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TESIS DOCTORAL

ESTRATEGIAS DE FISIOTERAPIA COGNITIVO CONDUCTUAL APLICADAS AL EJERCICIO EN PACIENTES CON MIGRAÑA CRÓNICA

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“No puedes esperar construir un mundo mejor sin mejorar a los individuos. Con este fin, cada uno de nosotros debe trabajar para mejorarse a uno mismo y, al mismo tiempo, compartir una responsabilidad general para con toda la humanidad, siendo nuestra responsabilidad particular ayudar a aquellos para quienes creemos que podemos resultar más útiles”

Maria Salomea Sklodowska-Curie

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ABSTRACT (English version)

In this doctoral thesis, chronic migraine is studied from different perspectives. The objective is to be able to have an alternative treatment to the pharmacological, in order to be able to study a treatment according to its neurophysiology and based on conservative techniques from the exercise under the bio-behavioral perspective.

For this, five studies have been carried out, with different methodological designs to not only study the hypothesis of the treatment of the disease but also to be able to study scientifically that the neurophysiological theories on which we support are based on a greater evidence.

In the first and second studies, a review of the scientific literature on biobehavioral techniques of education and therapeutic exercise is done. In the third and fourth studies, cross-sectional studies are intended to study the pathophysiology of chronic migraine by studying somatosensory and psychosocial variables associated with the disease to study the relationship between them. In the last one , a randomized clinical trial evaluates the combination of biopsychosocial techniques which are most effective for the treatment of chronic migraine. In the last study, these techniques are compared with a control group that only receives medication.

The results show that the pathophysiology of migraine is based on the central sensitization theory through the trigeminal-cervical nucleus also that biobehavioral treatments based on therapeutic education and exercise and the combination between them or with manual therapy or with medication are effective and safe approaches for the treatment of chronic migraine at least in the short term.

RESUMEN (Versión en castellano)

En la presente tesis doctoral se estudia la migraña crónica desde diferentes perspectivas. El objetivo es poder tener una alternativa de tratamiento al farmacológico, para poder así estudiar un tratamiento acorde con su neurofisiología y basado en técnicas conservadoras desde el ejercicio bajo la perspectiva bioconductual.

Para ello se han realizado cinco estudios, con diferentes diseños metodológicos para no solo estudiar la hipótesis del tratamiento de la enfermedad sino también para poder estudiar científicamente que las teorías neurofisiológicas en las que nos apoyamos se basan en una mayor evidencia.

En el primer y segundo estudios, se hace una revisión de literatura científica de las técnicas bioconductuales de educación y ejercicio terapéutico. En el tercer y cuarto estudios se pretende mediante estudios transversales, estudiar la fisiopatología de la migraña crónica estudiando variables somatosensoriales y psicosociales asociadas a la enfermedad, para estudiar la relación que existe entre ellas. En un último estudio se valora mediante un estudio clínico aleatorio qué combinación de técnicas biopsicosociales son más efectivas para el tratamiento de la migraña crónica, en este último estudio, se comparan éstas con un grupo control que únicamente recibe medicación.

Los resultados muestran que efectivamente la fisiopatología de la migraña se basa en la teoría de una sensibilización central, producida mediante el núcleo trigémino-cervical, y que los tratamientos bioconductuales basados en la educación terapéutica y el ejercicio y la combinación de estos entre ellos o con terapia manual y medicación, son abordajes efectivos y seguros para el tratamiento de la migraña crónica al menos a corto plazo.

CHAPTER 1. Theoretical background of Migraine and Pain

1. MIGRAINE

1.1. Classification

The international Classification of Headache Disorders (ICHD) is a document edited by the International headache society (IHS). IHS was established in London in 1982 with the objectives of making scientific advance in headaches, and improving the evaluation, education, promotion and knowledge of headaches around the world. IHS is made by 100 countries and a total of 1300 members (Belvis, Mas, & Roig, 2015). In 1988 edited the first diagnostic headache guide (Granella et al., 1994), in 2004 a second one ("Headache Classification Subcommittee of the International Headache S. The International Classification of Headache Disorders: 2nd edition," 2004), and more recently, 2013, the third one (Road, 2013).

Migraine is a common and incapacitating neurological disease (Road, 2013). According to the 3rd headache classification by the International Headache Society (Road, 2013), migraine is a common disabling primary headache disorder with high prevalence, socio-economic and personal impacts. The most frequent primary headaches are migraines and tension type headaches (Rasmussen, Jensen, Schroll, & Olesen, 1991).

Migraines are characterized by paroxysmal attacks of a unilateral throbbing headache (Latimer, 2013; Pozo-rosich, 2012) that may be associated with dysfunction of the autonomic nervous system (Bashir, Lipton, Ashina, & Ashina, 2013; Volcy, 2013).

Migraine is subdivided into 2 types: migraine without aura, which is characterized by headache with specific qualities, and migraine with aura, which has neurological symptoms that can precede or accompany the headache (Road, 2013). Aura is a transient neurological symptom which come before migraine in about 60 minutes. It consists in visual disruption or a prickling sensation around lips, tongue or half face.

Patients with chronic migraines suffer from headaches occurring at least 15 days per month for more than 3 months. These patients exhibit the features of a migraine attack for at least 8 days per month (Latimer, 2013; Pozo-rosich, 2012; Road, 2013). Episodic migraine leads with headache pain less than 15 days per month (Road, 2013)
Symptoms associated with migraines include sweating, allodynia, photophobia, phonophobia, vomiting and nausea (Bigal et al., 2008; Katsarava, Buse, Manack, & Lipton, 2012; Natoli et al., 2010; Road, 2013).

Schwedt et al., (Schwedt et al., 2015) observed patients with episodic and chronic migraine to determinate the surface, thickness and cortex volume by MRI. The results showed more activation in chronic migraine of the superior temporal gyrus which leads with neck and head movements; it could explain neck stiffness during migraine attacks. Prefrontal cortex, related with executive function which links with psychosocial variables associated to chronic migraine and insula; it is believed to process convergent information to produce an emotionally relevant context for sensory experience. With episodic migraine, the activation of cortical areas was more related to pain than to emotional ones.

Migraine associated comorbidities are related to disability and a decrease in the quality of life, as patients experience suffering, anxiety, depression, and some come to have obesity, cardiovascular diseases and fibromyalgia and other chronic diseases (Burshtein, Burshtein, Burshtein, & Rosen, 2015; Sullivan, Cousins, & Ridsdale, 2016)

1.2. Epidemiology: Prevalence and Incidence

Prevalence is defined as the proportion of a given population that has migraine over a period of time. Nowadays headaches are a worldwide health problem. More than 50 %

of European adult population suffered from headache in 2013, with migraine accounting for at least a 15%. 4% of the adult population suffer from chronic pain more than 15 days per month (Stovner & Andree, 2010). Migraine prevalence is higher in women, with its impact in higher among 20-50-year-old women. Additionally is lower in the elderly (Stovner, Zwart, Hagen, Terwindt, & Pascual, 2006).
In the Global Burden of Disease Survey 2010, Migraine was ranked as the third most prevalent disorder and seventh-highest specific cause of disability worldwide (Road, 2013).

The global burden of disease in USA 2017 classifies migraine as the most common of human afflictions (Gooch, Pracht, & Borenstein, 2017). Migraine and severe headache affect up to 72 million Americans, which represents 22.7% of the general population (Smitherman, Burch, Sheikh, & Loder, 2013). Migraine prevalence alone is estimated at 16.2% in adults, and is more prevalent in younger patients, particularly women (26,1%), although is still very common in elderly between 65-74 (18.7%), and also among the economically disadvantaged (Munakata et al., 2009; Smitherman et al., 2013). A chronic Migraine sufferer´s annual cost in 2014 was estimated at $9,364 with lost work productivity around 70% of the total account, because migraine is most frequently presented during prime working years (R. B. Lipton, Stewart, & von Korff, 1997; Munakata et al., 2009; Natoli et al., 2010; Payne et al., 2011). The total per person with episodic migraine was estimated at $2,158. Data from the National Health and Nutrition Examination Survey (NHANES), which is a program of studies designed to assess the health and nutritional status of adults and children in the United States, estimated a total cost of $ 78 billion per year.

Studies have also shown that each year 2.5% of patients who have episodic migraines develop into chronic migraine sufferers (Bigal et al., 2008).

Prevalence of migraine may change by sociodemographic features, as for example race. A population based study compared the prevalence of migraine among Caucasians, African-Americans, and Asian-Americans in the United States; results showed that it was lowest in Asian-Americans (female 9.2%, male 4.8%), intermediate in African-

Americans (female 16.2%, male 7.2%), and highest in Caucasians (female 20.4%, male 8.6%) (Stewart, Lipton, & Liberman, 1996).
In Spain the prevalence rates vary significantly, from 7.6% in Navarra to 18% in the Canary Islands (Younger, 2016). Lara et al., (Lara et al., 2015) reported migraine as the burden of neuropsychiatric disorders at 18.4% of all causes of DALYs (Disability-Adjusted Life-Years) generated in 2010 in Spain, the top five were depressive disorders, Alzheimer disease, migraine, substance use disorders, and anxiety. These five accounted for 70.9% of all DALYs according to neuropsychiatric disorders.

Incidence is defined as the rate of onset of new cases of disease in a defined population. Studies showed that the incidence of migraine with aura in males peaked at 5 years of age with an estimated rate of incidence of 6.6 per 1000 persons-years. Patients without aura peaked at the age of 10 to 11 years with an estimated 10 per 1000 person-years, new cases being uncommon in men at their 20s. In females it´s different, they have migraine with aura peaking at 12 to 13 years with an incidence rate of 14.1 per 1000 persons-years, and at the age of 14 to 17 with an incidence of 18.9 per 1000 persons-years (Stewart, Lipton, Celentano, & Reed, 1992; Younger, 2016).

According to years lived with disability (YLDs) migraine ranked 19th as a leading cause and represents 1.4% of the total causes of YLDs by WHO 2001 annual report (Leonardi, Steiner, Scher, & Lipton, 2005). In 2013 migraine represented a 46.1 change increase in YLDs from 1990 to 2013, and a change in standardized YLDs from 1990 to 2013 of 35.1%.

1.3. Biological, psychological and enviromental factors

Primary Headaches represent a large social and economic impact being one of the diseases that leads to more time off from work in the western hemisphere (Edmeads & Mackell, 2002; R. B. Lipton, Stewart, & Simon, 1998; Volcy-Gomez, 2006)
Migraine is a disabling neurological disease that concerns to the whole individual´s life fields (2,3) and is considered a complex condition based on the interaction of biological, psychological, and environmental factors (Frank Andrasik, Buse, & Grazzi, 2009; Gerber & Schoenen, 1998; Grazzi & Bussone, 2011). Some authors suggest that it is a biobehavioral disorder (Gerber & Schoenen, 1998; Grazzi & Bussone, 2011), result of a

determined cortical hypersensitivity and an associated social learning process (Gerber & Schoenen, 1998). Behavioral habits and medication intake due to migraine attacks are important factors to keep in mind.

According to Carlson, the biobehavioral approach for management of chronic craniofacial pain recognizes the importance of psychosocial factors, such as past history of pain, ongoing emotional states, health beliefs, and coping skills, that interact with the physiologic disturbances in determining the pain experience for the patients (Carlson, 2008).

Psychological suffering and pain have been associated with the development of depression or anxiety in patients with migraines (Press, 2015). Moreover, the comorbidities typically associated with migraines include disability, depression, anxiety, psychosocial impairment and bio-behavioral disorders (Finocchi, Villani, & Casucci, 2010; Ruscheweyh, Müller, Blum, & Straube, 2014).

This chronic disorder causes an imbalance in quality of life for sufferers (Valade, 2013; Zandifar et al., 2013). Chronicity affects the reduction in quality of life more so than the pain itself (Pozo-rosich, 2012).

Chronic migraine (CM) is also characterized by strong attacks of headaches, nausea, photophobia, vomiting, sleep disorders and psychosocial disorders (de Tommaso et al., 2014). CM is considered one of the most significant causes of disability worldwide (Ghajarzadeh et al., 2014). Numerous studies have shown that individuals who experience CM have considerable social impairment (Ghajarzadeh et al., 2014; Stuginski-Barbosa, Dach, Bigal, & Speciali, 2012).

Migraine also impacts not only in the sufferer patient but also in their families. There were only a few studies assessing the migraine impact in patients family, from the point of view of the cohabitating family members. They reported a moderate to severe effect of migraine in social and leisure activities as well as on family life (R. Lipton et al., 2003; MacGregor, Brandes, Eikermann, & Giammarco, 2004; Smith, 1998).

A recent study (Buse et al., 2016) assess the impact of migraine in family members from the perspectives of the person with migraine, her or his domestic partner and children. The results showed that people with migraine reported a higher family burden due to migraine than their partner did, a reduced participation in family activities due to migraine at least in 1 time a month, and it depends on headache frequency. Many of the patients believe that their partner did not believe in the severity or impact of their pain, and the feelings that they could be better parents without headaches.

1.4. Treatment Approaches

From a therapeutic point of view, the approaches for migraine can be classified as: pharmacological and non-pharmacological.

1.4.1 Pharmacological

According to medication consumption there are considerable differences between countries. In the US 23% of the chronic headache patients consume drugs everyday (Scher, Lipton, Stewart, & Bigal, 2010), while in northern Europe only a 9% of chronic migraine population does (Kristoffersen, Grande, Aaseth, Lundqvist, & Russell, 2012). It has been proved that the effectiveness of medication is higher in acute migraine than in the chronic one (Haag, 2011). Besides the fact that drugs vary, it is important to take into account risk of medication abuse, and the use of low scientific evidence treatments (Kristoffersen et al., 2012).

Treatment strategies for acute migraine include ; a stratified care, a step care within an attack and a step care across attacks (R. B. Lipton et al., n.d.). In the stratified care, medication election is based on attack severity, presence of nausea or vomiting, and degree of disability related to migraine. The step care within an attack is usually treated with nonsteroidal anti-inflamatory drug (NSAID), and if it fails, triptan is the election some hours later. For the step care across attacks, there is an initial medication based on the relief of symptoms (nonspecific analgesic) if it does not work clinicians prescribed another medication such as a triptan or dihydroergotamine (DHE) (Pringsheim, Davenport, Marmura, Schwedt, & Silberstein, 2016).

When migraine is chronic (CM), there are to kinds of medication election based on acute phase of migraine or the chronic one. For the acute phase the medication election is very similar to those used in episodic migraine, being based on the improvement of the symptoms (Silberstein, Dodick, & Pearlman, 2010). NSAIDs, triptans, DHE and antihemetics are used to treat CM, opiates should be avoided because of medication dependency and risk of medication overuse headache (Bigal et al., 2008).

Preventive treatment for chronic migraine has studied deeply and only a few medications have been proved effective (Cho, Song, & Chu, 2017). For example, botulinum toxine A (BOTOX-A) and topiramate have been shown to be effective in several randomized control trials (H-C Diener et al., 2007; H. Diener et al., 2010; Dodick et al., 2010; Silberstein et al., 2007; Silvestrini et al., 2003),. Other drugs as valproate, gabapentin, amitriptiline and tizanidine have been proved effective only in one RCT each of them (Couch & Amitriptyline Versus Placebo Study Group, 2011; Saper, Lake, Cantrell, Winner, & White, 2002; Spira, Beran, & Australian Gabapentin Chronic Daily Headache Group, 2003; Yurekli et al., 2008). There is no evidence for the serotonin reuptake inhibitors or serotonin and norepinephrine reuptake inhibitors as effective drugs for preventive phase of CM (Moja, Cusi, Sterzi, & Canepari, 2005). Otherwise, calcitonine gene-related peptide is believed to be effective for preventive CM treatment (Cho et al., 2017).

A combination of pharmacological and non pharmacological approaches have been considered the better way to manage migraine as well as in the whole chronic pain patients (Frank Andrasik, 2004). Stanos et al., concluded that the best treatment for chronic migraine was a multidisciplinary treatment including bio-behavioral and pharmacological approaches (Stanos, 2012).

In addition, patients who abuse medications exhibit a chronicity of pain that is clearly manifested (Pozo-rosich, 2012).

Patients with CM can consume a high quantity of drug products, which can lead to secondary headaches due to medication abuse (Biagianti, Grazzi, Usai, & Gambini,

2014; Suh, Park, & Shin, 2012) . Evers et al. (Evers et al., 2006) showed that no drug is superior with regard to headaches. The lack of treatment homogeneity is explained by the controversy regarding the pathophysiology of migraines (Cioffi et al., 2014b)

1.4.2 Non pharmacological

Non- pharmacological treatments for the treatment of migraine could be cognitive behavioral therapy (stress management training), biofeedback therapy, and relaxation training are recommended behavioral modalities with grade A evidence. Other treatment options are occipital nerve neurostimulation, transcranial magnetic simulation, non-invasive vagal nerve stimulation, supraorbital transcutaneus stimulation and sphenopalatine ganglion stimulation, which have shown promising results, but are not deeply investigated yet (Cho et al., 2017).

- Psychological interventions

Evidence showed that migraine may be comorbid with psychiatric conditions, notably anxiety and depression (Hamelsky & Lipton, 2006). Evidence supports the efficacy of psychological interventions in migraine (Sullivan et al., 2016).
There have been created a variety of biobehavioral therapies inside biopsychosocial model focus on the motor efferent mechanisms as, for example, therapeutic exercise as well as pain modulation mechanisms and therapeutic education based on pain neurophysiology. Their objective is the modulation of psychosocial factors, pain and disability (Nijs et al., 2014).

Biobehavioral approaches have four key components that could been used by clinicians: education, skills acquisition, skills consolidation and generalization and maintenance (Dennis C Turk).

Biobehavioral treatments (BBT) for chronic pain patients, includes education and self-care, cognitive behavioral interventions, and biobehavioral training (biofeedback, relaxation training, and stress management) (Frank Andrasik et al., 2009; Carlson, 2008; Rains, Penzien, McCrory, & Gray, 2005). BBT will help the patient to make adaptive thoughts about their condition as well as make changes in maladaptive pain behaviors to healthy behaviors. The treatments are design to help patients to manage their symptoms

and also their lives (Sluka & Turk, 2009).

- Therapeutic exercise

Therapeutic exercise according to the American association of physical therapy involve physical activities design to get some specific therapeutic goals. Its purpose is the restoration of musculoskeletal illness, decrease pain intensity, the prevention of diseases and to improve well-being ("Guide to Physical Therapist Practice. Second Edition. American Physical Therapy Association.," 2001). Among therapeutic exercises, cervical stabilization exercises or aerobic exercises have been used. Cervical stabilization exercises are made by light resistance weight with the objective of training or establishing neuromotor control in cervico-scapular and craniocervical regions (Falla, Rainoldi, Merletti, & Jull, 2003). This kinds of exercises have been associated with local and widespread hypoalgesia in adults with chronic pain (Naugle, Fillingim, & Riley, 2012; O'Leary, Falla, Hodges, Jull, & Vicenzino, 2007). There is not enough evidence yet about the effectivity of these kinds of exercises in the primary headaches environment (Biondi, 2005).

Therapeutic exercise is made by different kinds of exercise as graded activity (GA), graded exposure (GE) and motor control exercise (MC). Previous systematic reviews have demonstrated that GA, GE and CM are not more effective than other kinds of therapeutic exercise or manual therapy in pain intensity reduction or disability in chronic low back pain patients (López-de-Uralde-Villanueva et al., 2015; Macedo, Maher, Latimer, & McAuley, 2009).

- Therapeutic patient education

Education in pain neurophysiology is about a combination of therapeutic interventions with the objective of reconceptualizing pain, its function and which are the biological processes of pain support, differentiating it from other education as, for example, the cognitive behavioral therapy is (G. Lorimer Moseley & Butler, 2015). Previous studies have proven that therapeutic education is effective in acute and subacute low back pain, however it is not yet proven for chronic pain (Engers et al., 2008).

Educational interventions focused on biobehavioral approaches have been used to

reduce pain and improve quality of life in migraine sufferers as regards to finding a better way to treat chronic pain patients, because migraine patients have a difficulties managing pharmacological treatment (Evers et al., 2006). Therefore, the current study focuses its BBT on TPE.

The World Health Organization defined TPE as an education directed by health care providers trained in the education of patients in order to provide the patients' knowledge about the treatment of their disease condition, as well as to obtain the skills to avoid complications while acquiring balance in their lives to improve or maintain their quality of life (Daviet et al., 2012; Reed, 2010; WHO Working Group, 1998). TPE is designed to train patients in self-managing skills, in adapting the treatment to their specific chronic disease, and in coping abilities and processes (Reed, 2010).

TPE provides contact between the care providers and patients (Daviet et al., 2012) to allow patients to become autonomous in the long term by offering the psycho-pedagogic means that are essential to motivate patients to treat themselves (Reed, 2010).

According to Golay et al., motivation, which is a state of activation in order to improve quality of life, includes an increment of compliance providing knowledge by "trial and error," as well as cognitive conflict or expression. It means that change comes from the within the patient, who becomes the author of his or her own learning process (Reed, 2010).

Daviet et al. (Daviet et al., 2012), who studied TPE for stroke survivors, reported that TPE improves stroke survivor's understanding about their chronic disease and also improves mood and satisfaction levels, which changes their lifestyle after the education approach (Reed, 2010).

TPE has been extensively studied in the management of anxiety, stress, and pain for chronic lower back pain (Louw, Diener, Butler, & Puentedura, 2011a). It is thought that in chronic diseases, TPE should be adapted to the needs of patients and caregivers

(Daviet et al., 2012).

BBT have been verified and have "grade A" evidence in the American consortium of Evidence Based Headache Guidelines (R. Nicholson, Nash, & Andrasik, 2005a). It has been proposed BBT based on educational approaches to manage migraine (Buse & Andrasik, 2009). Nevertheless, there does not exist any systematic review and meta-analysis published in the last years.

- Manual Therapy

Physical therapies including spinal joint manipulation/mobilization, interventions for soft, therapeutic exercises and needling therapies are proposed to be effective for the management of some headaches. The effectiveness of these interventions will depend on clinical reasoning because all interventions are not equally effective for all headache pain conditions. Evidence of physical therapy in migraine is more controversial than in TTH (Tension type headache), because migraine pathogenesis involves activation of sub-cortical structures and the trigeminal-cervical system, and pathogenesis of TTH is more associated with musculoskeletal disorders (Fernandez-de-las-Penas & Cuadrado, 2016) .

Manipulation and mobilization have been demonstrated both physiologic and mechanical effects including analgesic effects, motor effects and sympathetic nervous system effects in chronic epicondylalgia pain (Paungmali, O'Leary, Souvlis, & Vicenzino, 2004). It has been shown that spinal manipulation/mobilization is effective in adults for migraine and cervicogenic headache (Gert Bronfort, Haas, Evans, Leiniger, & Triano, 2010).

Manual therapy combined with functional, endurance, and strengthening exercises produced greater reductions in pain and improvements of function than both manual therapy or exercise isolated in chronic pain patients (Hoving et al., 2006; Walker et al., 2008).

Effectiveness of manipulation and mobilization have been noted when combined with other approaches as for example exercise (Gross et al., 2010)

Approaches that mix therapeutic education, manual therapy and therapeutic education programs, have been showed better improvements than the approaches isolated in the treatment of chronic pain patients (Biondi, 2005).

2. PAIN

2.1. Pain and Physiophatology of Migraine

Pain could be classified as acute and chronic pain. Acute pain is made by tissue damage resulting in a sensory activation response of nociceptive the system. Phenomena mediated by an inflammatory response leading with a sensitization of peripheral receptors (Loeser & Treede, 2008).

Peripheral sensitization associated to acute pain is a process in which exist a decrement of detection thresholds, and nociceptors amplify its response, in order to protect damaged area. It means that peripheral sensorial neurons are exposed to inflammatory mediators in damaged tissue (Hucho & Levine, 2007). This acute pain and hypersensitivity in damaged areas is called primary hyperalgesia.

When pain spreads beyond an injury in non-damaged areas, it is known as secondary hyperalgesia including central mechanisms. Peripheral sensitization leads with alterations on thermal sensitivity while central one to alterations on mechanical sensitivity (Latremoliere & Woolf, 2009).

Central sensitization is associated to chronic pain, it is explained by neuroplastic changes that maintain pain sensation even when there is not any presence of potential damage. In this case there is a high neuronal activation in spinal cord and supramedullar neurons (Latremoliere & Woolf, 2009) . It is characterized by thresholds decrease and sensitivity increase, there are pain modulation mechanisms inefficiency (Meeus, Nijs,

Van de Wauwer, Toeback, & Truijen, 2008). Central sensitization could produce psychological stress, increasing the amplification of pain sensation (Curatolo, Arendt-Nielsen, & Petersen-Felix, 2006).

The causes and pathophysiology of migraines are still unknown despite recent studies investigating a mechanism of central sensitization in the trigeminocervical complex to explain the causes (Bartsch & Goadsby, 2003; Volcy, 2013).

The most recent lines of research have suggested that severe headache attacks involve the trigeminocervical complex (TCC) due to 2 underlying neuronal mechanisms: peripheral sensitization and central sensitization (Bartsch & Goadsby, 2003; Coppola, Di Lorenzo, Schoenen, & Pierelli, 2013; Goadsby, 2009).

The cervical trigeminal complex is composed of a convergence of neurons of the superior lamina of the caudal trigeminal nucleus nerve and the dorsal horns of C1 and C2 (Volcy, 2013) **Figure 1**.

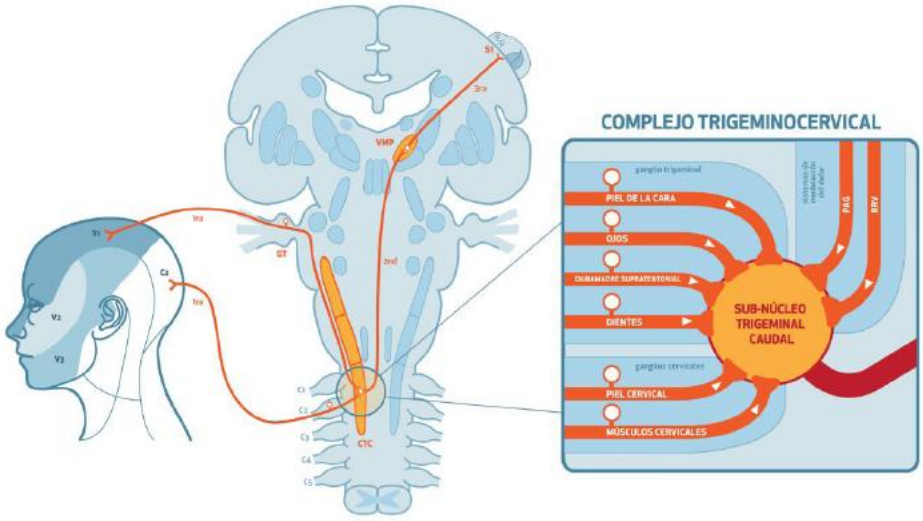


Figure 1. Graphic representation of trigeminal complex

Assignment of image by La Touche, Roy. Aspectos neurofisiológicos y biomecánicos de la región cervical sobre el dolor cérvico-craneofacial: Implicaciones del tratamiento y diagnóstico. Dirigida por Josúe Fernández Carnero y Carlos Goicoechea García. Tesis doctoral inédita. Universidad Rey Juan Carlos, facultad de ciencias de la salud, Madrid, 2014.

In this complex, the second-order nociceptive neurons and the first three cervical nerves converge (Bartsch & Goadsby, 2003). Patients with CM experience pain in territories

that belong to the division of the trigeminal and present various clinical conditions such as facial skin hypersensitivity, neck muscle sensitivity and hyperalgesia (Bigal & Lipton, 2008). This is theoretically due to the anatomical convergence of trigeminal afferent fibers and upper cervical nerves, as well as to the sensitization of second-order neurons, which receive nociceptive trigeminal primary afferent neurons, during headache attacks (Aurora, Kulthia, & Barrodale, 2011).

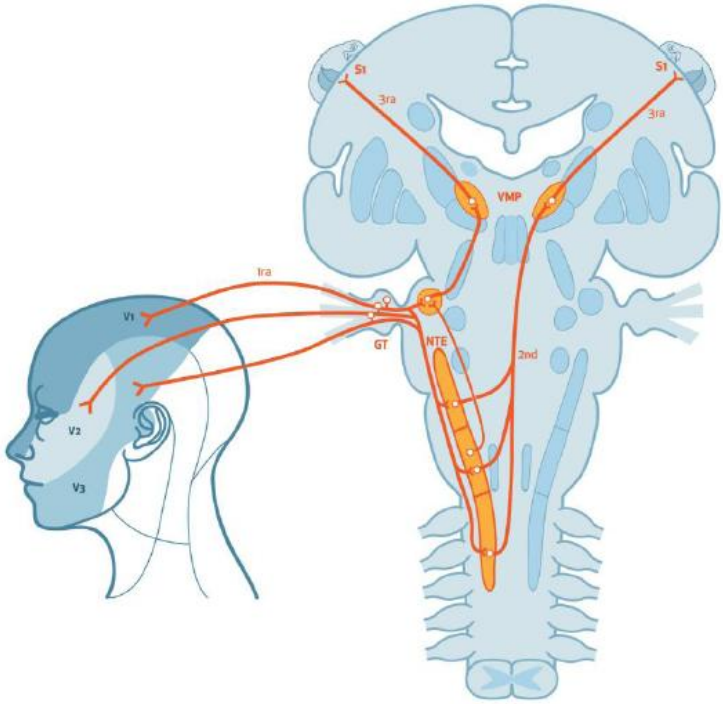


Figure 2: Neuroanatomic representation of trigeminal system from periphery to primary somatosensory cortex (S1), thalamus in Posteromedial ventral nucleus (VMP), trigeminal spinal nuclei / NTE; trigeminal ganglion (GT)
Assignment of image by La Touche, Roy. Aspectos neurofisiológicos y biomecánicos de la región cervical sobre el dolor cérvico-craneofacial: Implicaciones del tratamiento y diagnóstico. Dirigida por Josúe Fernández Carnero y Carlos Goicoechea García. Tesis doctoral inédita. Universidad Rey Juan Carlos, facultad de ciencias de la salud, Madrid, 2014.

Zapaterra et al., (2011) showed that patients with chronic headaches presented allodynia and lower outcomes of cutaneous pressure pain thresholds (PPTs) compared with chronic individuals who presented episodic headache (Zappaterra, Guerzoni, Cainazzo, Ferrari, & Pini, 2011). Moreover, patients with chronic and episodic migraines had lower PPTsv in some cranial and cervical muscles compared with healthy subjects (Débora Bevilaqua Grossi et al., 2011).

Other studies have shown that patients with CM have tenderness in the masticatory muscles (73%), neck tenderness (63%) and a greater prevalence of cervical pain than nausea (Anne H Calhoun et al., 2010; Stuginski-Barbosa, Macedo, Bigal, & Speciali, 2010). These findings suggest that there could be a pathophysiological relationship with other disorders, such as cranial-mandibular disorders, and therefore TCC sensitization (Marklund, Wiesinger, & Wänman, 2010b).

2.2. Biopsychosocial Characterization of Pain

2.2.1. Definition

Pain according to the International Association for the Study of Pain is defined as: "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". It means a physiological feeling and also a psychological reaction related to that sensation, which is not always produced by tissue injury although patients experience real pain.

Pain involves a perceptual process in the brain which in turn involves suffering, pain behavior and variable disability that may affect mood (D C Turk, 1997). Whether pain becomes chronic should be related to behavior, and to psychological and neurobiological factors (Apkarian, 2008; Hashmi et al., 2013b). A recent study shows how the chronification of back pain changes brain representation from nociceptive circuits to emotional ones, turning the acute pain pattern to as emotional distress (Hashmi et al., 2013b).

Psychological responses to pain are made up of patient´s personal and social experiences. The biopsychosocial characterization of pain imply three different terms that are dynamic, in continuous change (Gatchel, Peng, Peters, Fuchs, & Turk, 2007; Nijs, Paul van Wilgen, Van Oosterwijck, van Ittersum, & Meeus, 2011). The biological part means the genetically inherited characteristics about psychological functioning. According to psychological terms the right way to define this is thinking about mental and behavioral processes of the person, including cognition, emotion and motivation. The social aspect is determined by both the individual and environmental factors influenced by patients family, community, culture and society (Sluka & Turk, 2009; Dennis C Turk).

2.2.2. History/evolution

Before the 1960s, pain was understood to be a sensation based on its physiology, deriving from an illness or disease but not really important. In 1965 Melzac and Wall developed a new theory about pain mechanisms. It was called the " Control Gate Theory" which emphasized the brain´s regulation of nociceptive pain transmission (R Melzack & Wall, 1965). This theory suggested that pain was different from another sensations because it was a multidimensional experience, with a afferent pathway from the peripheral nerve responding to a noxious stimulation and the descending tracks from the cortex to the spinal cord. But during the second half of the 20th century, it was realized that this theory didn´t explain pain experience properly. Melzac developed a new concept about pain biophysiology, " the Neuromatrix" (R Melzack). Neuromatrix theory explains that pain is produced by the output of a neural network in the brain instead of a sensory input evoked by inflammation, injury or other pathology or diseases (R Melzack, 2001; Ronald Melzack, 2005). This theory brings up the existence of circuits made of several neural structures that makes a neurosignature which explains the multidimensional experience of pain (R Melzack; Ronald Melzack, 2005; Ronald Melzack & Katz, 2013). The multidimensional experience of pain includes three dimensions: the sensory/discriminative, the motivational/affective and the cognitive/evaluative dimensions: the sensory/discriminative dimension would be directly related to anatomophysiological mechanisms. The motivational/affective dimension involves subjective quality of the experience of pain , particularly in aspects of suffering , or emotional changes. The cognitive- evaluative dimension is directly related to the motivational/affective and refers to beliefs, cultural values and cognition , such as self-efficacy , perceived control and the consequences of the pain experience variables.

Pain experience variables may be classified in two groups: the affective factor which includes anger, depression and anxiety and the cognitive factor involving coping strategies, pain catastrophizing, Kinesiophobia, beliefs about pain, self-efficacy, acceptance and so on. There is also the fear-avoidance model which also explains why the pain patients experience is an affectation in their quality of life and pain chronicity (Vernon, Guerriero, Kavanaugh, Soave, & Puhl, 2013; Vlaeyen & Linton, 2000).

Biopsychosocial treatment strategies for pain may include a wide range of interventions, among others physical therapy based on therapeutic patient education about the neurophysiology of pain (Gallagher, McAuley, & Moseley, 2013; P. Kindelan-Calvo et al., 2014; Meeus, Nijs, Hamers, Ickmans, & Oosterwijck, n.d.-a; Meeus, Nijs, Van Oosterwijck, Van Alsenoy, & Truijen, 2010; Nijs et al., 2011), graded motor imagery (Bowering et al., 2013; G L Moseley, 2004; G Lorimer Moseley, 2006), manual therapy (22–24), and therapeutic exercise (Alfonso Gil-Martínez et al., 2013; Senlöf, Denison, & Lindberg, 2009) and the combination of these approaches has been demonstrated effective in the treatment of pain patients (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, & La Touche, 2015; Cleland & Palmer, 2004; Hedborg & Muhr, 2012)

2.2.3. Biopsychosocial Model

Psychological responses to pain fit a patient´s personal and social spectrum. The psychological factors determine mechanisms and strategies in pain management. These psychological factors could commence an illness, maintain it or contribute to start secondary reactions related to illness or diseases.

The biopsychosocial point of view is divided in three groups, the biological, psychological and social. Biological part of the biopsychosocial model of pain includes the genetically inherited characteristics of individuals psychological functioning. The psychological is made by mental processes and behaviors which could be explained by cognition, emotion and motivation. The social is influenced by an individual´s family, community, society and culture. The biopsychosocial model is dynamic, which means that it is in continuous change (Dennis C Turk; Turk DC, 1999).

The biopsychosocial model are based in the cognitive-behavioral model, which suggest that actions or individual behaviors (adaptive and maladaptive) are developed and maintained across conditioning and social learning processes. Cognitive models are based in individuals thoughts about pain or illness. The social dimension of behavioral and affective responses are learned and are understood by others via social knowledge principles (Ho, Peng, Lai, & Chan, 2001; Steklis & Walter, 1991; Dennis C Turk).

Psychological adaptation to pain is made up for the cognitive assessment, emotional and behavioral response.

The psychological reaction is explained by a normal response or a pathological one, with its pertinent adjustments (see figure 3)

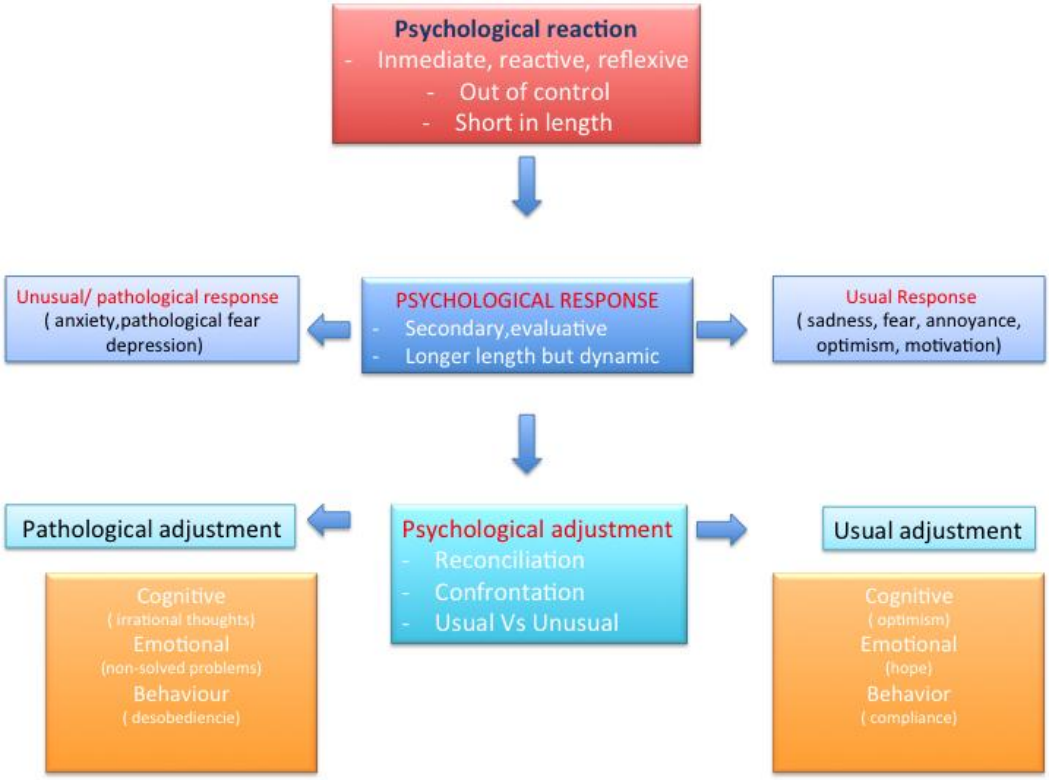


Figure 3: Psychological reaction

Psychological factors associated to pain conceptualization are the emotional factors (depression, anxiety, anger) and the congnitive variables (beliefs, auto-efficacy, catastrophizing, confrontation and acceptance). There is also important to take in account the personality factors (Turk DC, 1999).

The biopsychosocial model help researchers and clinicians to clarify complex pain symptom presentation and answer difficult clinical questions in order to investigate functional, social, affective, and cultural components that may help to explain complex pain presentations (F Andrasik, Flor, & Turk, 2005; Engel, 1981; Turk DC, 1999).

The biopsychosocial approaches are important because these are the way that patients

receive a wide range of interventions (cognitive behavioral therapy, physical therapy, biofeedback, occupational therapy) that address specific biopsychosocial dimensions of pain. These interventions provide a broad knowledge based on health treatment as psychosocial and lifestyle changes (Stayner, S., Ramezani, A., Prasad, R., and Mahajan, 2016).

- Neuroaffective Theories

The neuroaffective theories of pain propose that group dynamics, complex emotions, affect mediated by socialization, , and pain share common neurological pathways that are simultaneously activated. Emotions derived from social fighting and physical pain evolved and co-developed in the brain for the purpose of preventing social separation (Eisenberger & Lieberman, 2004). When a person experience social isolation or social exclusión, the dorsal region of the anterior cingulate gyrus of the brain, the same brain region that is responsible for the affective components of pain, has an activity increase (Eisenberger, Lieberman, & Williams, 2003). Furthermore, empathy in response to another individual pain also shares similar neuroanatomical regions (Lamm, Decety, & Singer, 2011; Novembre, Zanon, & Silani, 2015). This suggests that socially mediated emotions are essential to consider in clinical and research practice.

The Theory of Mind is a neuropsychological theory that suggests that individuals deduce what other people think, feel, desire, by the process of self-analysis (Baron-Cohen, 1991) . This theory also suggests shared neural pathways with empathy and pain. Brain imaging studies indicate that perception of other's emotional and physical pain show changes in the bilateral anterior areas of the thalamus and in the anterior middle cingulate cortex; physical pain shows changes in the left insula; and emotional pain shows changes in the dorsomedial prefrontal cortex (Bruneau, Pluta, & Saxe, 2012).

- Neurocognitive Theories:

Theories of attention and pain suggest that attention networks and working memory load are influenced by pain and also share structures as, for example, the dorsal lateral region of the frontal, somatosensory areas of the parietal, anterior cingulate gyrus (Legrain et al., 2009). Hyper-attentiveness to physical sensation can lead to a very high response to pain stimuli. The increase of attention to pain stimuli leads to brain activity

in central pain regions. A low attention or distracting attention away from pain stimuli can lead to brain deactivation of central pain regions (F Andrasik et al., 2005). In addition to attention and working memory disruptions, pain also impacts other cognitive processes such as executive function, learning, and memory retrieval, which may further reflect frontal and subcortical dysregulation observed in pain sufferers (Heyer et al., 2000; Martelli, Grayson, & Zasler, 1999; Franco Mongini, Keller, Deregibus, Barbalonga, & Mongini, 2005).

- Neuropsychological Models

The biopsychosocial model is an extensive paradigm for pain specialists to identify cognitive and affective models of pain. Advances in brain imaging studies and new neuropsychological theories of pain further complement the biopsychosocial model. Neuropsychological theories of pain primarily focus on the shared neural networks between brain function and pain processing. Neuropsychological theories of pain primarily encompass neurocognitive and neuroaffective theories. The neurocognitive and neuroaffective models of pain also build upon earlier brain-pain theories (e.g. Specificity/Localization Theory, Pattern Theory, Neuromatrix Theory, and Gate-Control Theory).

- Emerging Brain Connectivity and Reorganization Models:

Theory of functional cortical connectivity and reorganization refers to how the brain changes as a result of experiencing pain. When acute pain becomes chronic, localized nociceptive brain activity shifts to emotional brain circuits' activity and reduction in hippocampal-medial frontal lobe connectivity (Baliki et al., 2012; Hashmi et al., 2013a; A. A. Mutso et al., 2014) These indicate that affective-neurocognitive factors are not only involved in the interpretation of pain, but that the constructive meaning the brain assigns to the pain over the course of time changes the way in which the brain processes pain information. Furthermore, the transitioning point of going from acute pain to chronic pain can have vast effects on the brain's processing networks.

In the following work we expect to make two reviews about two of the biobehavioral techniques that we consider the key in the chronic migraine treatment. Those approaches are the therapeutic exercise ad the therapeutic patient education. After study

the effectiveness of those techniques we would like to answer and clarify if it is possible, more clues about the physiopathology and migraine origin conducting two cross-over studies. We deeply believe that migraine origin has a hand on the sensitization of trigemino-cervical system and this proccess therefore bring a central and pheripheral sentitization in chronic migraine illness.

Other of the objetives in the present work is to determine if there exist a relationship between psychosocial and somatosensorial variables in patients with chronic migraine.

To sum up we would like to carry a randomized clinical trial in which we will able to determine which combination of biobehavioral approaches are the most effective to improve quality of life in chronic migraine patients.

CAPÍTULO 2. Ejercicio terapéutico como tratamiento de las migrañas y cefaleas tensionales: revisión sistemática de ensayos clínicos aleatorizados

1. INTRODUCCIÓN

Según la Asociación Americana de Fisioterapia, la terapia a través de ejercicio, o Ejercicio terapéutico (ET), consiste en un régimen o plan de actividades físicas diseñado y prescrito para lograr metas terapéuticas específicas. Su propósito es restaurar la función normal musculoesquelética o reducir el dolor causado por enfermedades o lesiones, así como prevenir estas lesiones y mejorar la sensación de bienestar ("Guide to Physical Therapist Practice. Second Edition. American Physical Therapy Association.," 2001). Algunos tipos de ejercicios utilizados de forma terapéutica han sido el tipo aeróbico o los ejercicios de estabilización cervical. Estos últimos consisten en un programa que se desarrolla con ejercicios de baja carga de resistencia con el fin de entrenar o reestablecer el control neuromotor de las regiones cervicoescapular y craneocervical (Falla et al., 2003). Además, dichos ejercicios se han relacionado con hipoalgesia general y local, respectivamente, en adultos con dolor crónico (Naugle et al., 2012; O'Leary et al., 2007).

A pesar de que la evidencia científica cada vez aporta más información de los efectos del ET, es fundamental que se siga investigando la efectividad de esta modalidad de tratamiento. Son necesarios estudios de mayor evidencia para establecer los efectos de

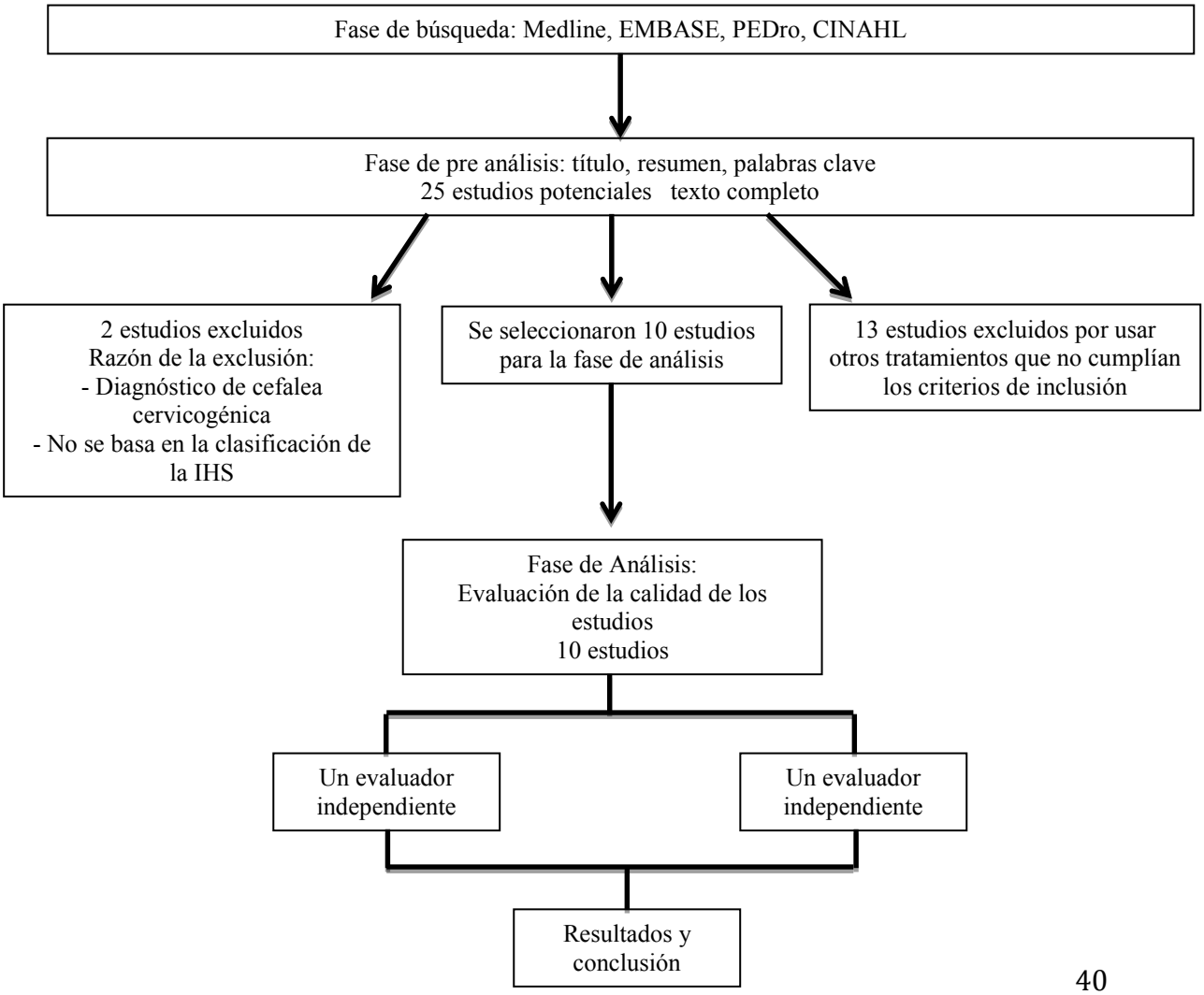
los ejercicios dirigidos en el campo de las cefaleas primarias (Biondi, 2005). En la actualidad, no existen revisiones sistemáticas que evalúen de forma específica la efectividad del ET en las migrañas o cefaleas tensionales (CTT).

El objetivo de esta revisión es el de analizar la efectividad que tiene el ET sobre las migrañas y las CTT según la información de ECA.

2. MÉTODO

2.1. Participantes

La revisión sistemática se realizó con un protocolo predefinido y subdividido en cuatro fases basado en las normas de la declaración PRISMA(David Moher, Liberati, Tetzlaff, & Altman, 2009) Ver ***Figura 4*** *debajo* – Diagrama de flujo



Los criterios de selección utilizados en esta revisión se basan en aspectos metodológicos y clínicos tales como el tipo de estudio, la población de estudios, las intervenciones y medidas para los resultados.

- *Pacientes*

Los pacientes de los ensayos seleccionados debían ser mayores de 18 años, diagnosticados de migraña y/o CTT según la clasificación de la ICHD y con síntomas crónicos de más de seis meses.

2.2. Variables e instrumentos

- *Tipo de estudios*

Se seleccionaron ensayos clínicos controlados aleatorizados (ECA) que presentasen comparaciones con un grupo control u otras intervenciones debidamente protocolizadas. Únicamente los estudios publicados en los idiomas inglés y español fueron incluidos. La fecha de las publicaciones fue restringida al periodo 1979-2012.

- *Intervención terapéutica*

Fueron incluidos ECA donde las intervenciones principales se basaran en ET combinado o no a otros tratamientos de fisioterapia.

- *Medidas de los resultados*

Las medidas para comprobar los resultados y efectos del tratamiento debían valorar al menos dos o más variables relacionadas con: intensidad del dolor, discapacidad o medidas de calidad de vida, además estas tuvieron que ser registradas a corto plazo (después del último tratamiento), medio plazo (aproximadamente 3 meses) o largo plazo (aproximadamente 6 meses).

– *Estrategia de Búsqueda*

Se realizó una búsqueda de artículos científicos utilizando las bases de datos MEDLINE (1979-2012), EMBASE (1979-2012), PEDro (1979-2012) y CINAHL (1979-2012) finalizando dicha fase en el transcurso del mes de agosto del 2012. Los términos utilizados para la búsqueda fueron derivados de la combinación de las siguientes palabras: “Primary headache”, “Migraine with Aura”, “Migraine without Aura“,

"Tension Type Headache", "therapeutic education", "educational", "education", "exercise therapy", "exercise", "training programme", "craniocervical training", "exercise craniocervical", "physical therapy", "physiotherapy", "rehabilitation", "randomized control trial", "headache intensity", "Quality of Life", "headache frequency". La fase de búsqueda la realizaron dos revisores independientes utilizando la misma metodología y las diferencias que surgieron en esta fase se resolvieron por consenso.

2.3. Procedimiento

- *Criterios de selección y extracción de datos*

El primer análisis de información se realizó mediante dos revisores independientes que evaluaron la pertinencia de los ECA en relación con la pregunta y el objetivo de investigación. Este primer análisis se realizó basándose en la información del título, el resumen y las palabras claves de cada estudio. Cuando no había consenso o los resúmenes no contenían la información suficiente se accedió a revisar el texto completo. En la segunda fase de análisis, con el texto completo, se procedió a comprobar si los estudios cumplían todos los criterios de inclusión. Las diferencias entre revisores se resolvieron por un proceso de discusión/consenso moderado por un tercer revisor(Furlan, Pennick, Bombardier, & van Tulder, 2009). Los datos que se describen en los resultados se extrajeron por medio de un protocolo estructurado que garantiza la obtención de la información más relevante de cada estudio (Higgins JPT, 2011).

- *Valoración de la calidad de los estudios*

La valoración de calidad metodológica de los estudios se realizó mediante la lista Delphi(Verhagen et al., 1998), este instrumento se desarrolló por medio de consenso de especialistas quienes establecieron 10 criterios que valoran si: 1.- se realizó una distribución aleatoria, 2.-existió una adecuada ocultación de la asignación, 3.- los grupos de estudio eran similares, 4.- se especificaron de los criterios de la elegibilidad, 5.- se cegó al investigador que valoró el resultado, 6.- se cegó al investigador que realizó el tratamiento, 7.- se cegó al paciente, 8.- se presentaron las estimaciones de los resultados y las medidas de variabilidad y 9.- se realizó el análisis de la intención a

tratar. 10.- se añadió un criterio más basado en si se describió el índice de retiros y abandonos.

Los criterios metodológicos se calificaron de la siguiente manera: se cumple (1 punto), no se cumple (0 puntos) o no se sabe (0 puntos). La máxima puntuación posible es de 10 puntos con un rango de 0 a 10. Se consideran estudios de alta calidad cuando cumplen 6 o más criterios(van Tulder, Furlan, Bombardier, & Bouter, 2003). La lista Delphi presenta una buena validez concurrente con la escala Jadad (Spearman r =0.63 a 0.71) y una fiabilidad inter-evaluador entre 0,54 y 0,85(Olivo et al., 2008).

Dos revisores independientes analizaron la calidad de todos los artículos seleccionados utilizando la misma metodología, los desacuerdos entre revisores se resolvieron por consenso mediante la inclusión de un tercer revisor. La fiabilidad inter-evaluador se determinó mediante la utilización de coeficiente de Kappa (> 0,7 significa alto nivel de acuerdo entre evaluadores, entre 0,5 y 0,7 un nivel moderado de acuerdo, y <0,5 un bajo nivel de acuerdo)(Cohen, 1960).

- *Análisis cualitativo*

El análisis cualitativo utilizado en esta revisión se basó en la clasificación de los resultados según los niveles de evidencia científica(van Tulder et al., 2003). La evidencia fue categorizada en 5 niveles dependiendo de la calidad metodológica de los estudios, a continuación se presentan estos niveles: 1) *evidencia fuerte*, representa resultados de múltiples ECA con buena calidad metodológica; 2) *evidencia moderada*; representa resultados de múltiples ECA con baja calidad metodológica y/o de ensayos clínicos controlados (ECC) y/o un ECA de alta calidad; 3) *evidencia limitada*, representa resultados de un ECA y/o un ECC de baja calidad; 4) *evidencia contradictoria*, representa resultados contradictorios de ECA y/o ECC; 5) *No hay evidencia*, no existen ECA o ECC.

Un requisito indispensable para describir los resultados y conclusiones según los niveles de evidencia científica es que haya homogeneidad clínica y metodológica en los

estudios. Los resultados descritos en el formato que incluyen los niveles de evidencia se pueden observar en los apartados de resultados y conclusión.

3. RESULTADOS

Dentro de la búsqueda de artículos y en la primera fase de análisis se seleccionaron diez ECA(Castien, van der Windt, Grooten, & Dekker, 2011; De Hertogh et al., 2009; Dittrich et al., 2008; John, Sharma, Sharma, & Kankane, 2007; F Mongini et al., 2012; E. Soderberg, Carlsson, & Stener-Victorin, 2006; E. I. Soderberg, Carlsson, Stener-Victorin, & Dahlof, 2011; Torelli, Jensen, & Olesen, 2004; van Ettekoven & Lucas, 2006; Varkey, Cider, Carlsson, & Linde, 2011) de 25 inicialmente elegidos en la fase de pre-análisis. En todos los estudios, se realizó ET como modalidad principal de tratamiento y en algunos se combinó con intervenciones de fisioterapia para tratar las migrañas y/o las CTT. La ***Tabla I*** representa de forma descriptiva las características epidemiológicas de los estudios, así como los resultados y conclusiones de los autores de cada artículo. También se presentan los datos estadísticamente significativos más relevantes.

	n	Población y diagnóstico	Grupos de estudio	Mediciones/ variables	Seguimiento	Resultados/conclusión de los autores	Notas
Soderberg et al [32]	90	Edad: 37,5 años Hombre/Mujer: 17/73 CTC	Acupuntura (n = 30) Entrenamiento físico (n = 30) Relajación (n = 30)	Satisfacción Vitalidad Calidad del sueño	Antes del tto. Después del tto. 3 meses 6 meses	Todos reducen los síntomas de las CTC. El entrenamiento físico mejora de forma significativa a los 3 meses la calidad de vida respecto a los otros tratamientos (p = 0,04), y la relajación lo hace a los 6 meses con la intensidad del dolor y con la percepción de mejoría (p = 0,04)	Se utilizó el ITT
Soderberg et al [31]	90	Edad: 37,5 años Hombre/Mujer: 17/73 CTC	Acupuntura (n = 30) Entrenamiento físico (n = 30) Relajación (n = 30)	Intensidad del dolor (0-100) Períodos sin dolor (períodos/semana) Días sin dolor (días/semana)	Antes del tto. Después del tto. 3 meses 6 meses	Todos los tto. mejoran los síntomas de CTC. La relajación tuvo mayor efecto que los otros grupos en los períodos y días sin dolor de cabeza (p < 0,05 y p < 0,01, respectivamente)	ITT 2,5-3 meses de tto. Relajación: Larsson y Daleflod, Jacobson y Schultz
Van Ettekoven et al [33]	81	Edad: 46,5 años Hombre/Mujer: 82,5% M CTC y episódica	ECC (n = 39) GC: tratamiento clásico de fisioterapia	Frecuencia del dolor (días/semana) Intensidad del dolor (0-10) Escala de	Inicio 6 semanas 6 meses	La fisioterapia, incluyendo el ECC, reduce los síntomas de la CTC durante un tiempo prolongado. A los seis meses, el grupo	6 semanas de tto. GC: masaje, movilización pasiva

			y corrección postural (n = 42)	clasificación numérica (0-10) Duración del episodio (h/día) Calidad de vida SF-36 Escala multidimensional de locus de control para cefalea	de ECC, en comparación con el GC, redujo significativamente la frecuencia (p = 0,0001), intensidad (p = 0,001), duración (p = 0,011) e ingesta de medicación (p = 0,003).	según Maitland
Mongini et al [30]	18 81	Edad: 47 años Hombre/Mujer: 263/1.618 Cefaleas primarias, dolor miofascial y posibles mezclas	Ejercicios de hombro y cuello, ejercicios de relajación e instrucciones para evitar parafunción craneocervical (n = 909)	GC: autoadministración de un programa de ejercicio y educación en casa (n = 972) Intensidad del dolor (0-5) Frecuencia del dolor (%) Días al mes de cefalea y dolor de cuello/hombro (día/mes) N.º de analgésicos consumidos Índice de	Inicio 6 meses	El programa reduce la cefalea y el dolor de cuello y hombros en trabajadores, y parece ser fácilmente llevado en atención primaria. No hubo diferencias entre los grupos	

				dolor de cabeza (promedio de intensidad y frecuencia)			
John et al [29]	65	Edad: 34 años Hombre/Mujer: 16/49 Migraña sin aura	Terapia de yoga: relajación, estiramientos, ejercicios GC: 3 sesiones de educación y autocuidados (1 sesión/mes)	Frecuencia (día/mes) Máximo dolor (0-10) Mínimo dolor (0-10) Intensidad del dolor (1-10) Índice de dolor de cabeza Medicación Cuestionario McGill del dolor Escala de depresión y ansiedad hospitalaria	Inicio 3 meses	Significativa reducción de la frecuencia de la migraña y síntomas asociados en los pacientes tratados con yoga en un período de tres meses ($p < 0,001$)	Respiraciones de yoga: 5 días/semana Limpieza nasal: 1 día/semana
De Hertogh et al [27]	37	Edad: 43 años Hombre/Mujer: 9/28 Cefaleas primarias y cefaleas cervicogénicas	Movilización espinal y ejercicio terapéutico (n = 19) GC: tratamiento médico convencio	Efecto global percibido (1-7 puntos) Test de impacto de cefaleas (36-78 puntos) Frecuencia (veces/mes) Intensidad	Semana 7 Semana 12 Semana 26	Mejorías significativas en las medidas de ambos grupos comparadas con la línea base. Sin embargo, no hubo diferencias significativas entre los grupos	Tratados 30 min durante 6 semanas y hasta 12 sesiones

			nal (n = 18)	(EVA 0-100) Ingesta de medicación Uso de ayuda profesional extra			
Varkey et al [34]	91	Edad: 44 años Hombre/Mujer: 9/82 Migrañas con aura y sin aura Duración: 25 años	Relajación (n = 30) Ejercicio (n = 30) Topiramato (n = 31)	Frecuencia (días/mes) N.º de migrañas/mes Intensidad de dolor (EVA 0-100) Dosis de medicación/mes Calidad de vida (1-100) Nivel de actividad física (min/semana) Sedentarismo (h/día) Consumo oxígeno (mL/kg/min)	Al terminar tto. 3 meses 6 meses	No hubo diferencias significativas entre grupos. El ejercicio puede ser una opción para el tto. profiláctico en aquellos pacientes que no se beneficien o no quieran tomar medicación diariamente	ITT Algunas medidas de variables sólo se recogen después del tto.
Dittrich et al [28]	30	Edad: 33 años Hombre/Mujer: 0/30 Migrañas	Ejercicio aeróbico GC: información sobre el efecto de la actividad	Intensidad del dolor (0-5) Frecuencia (veces/semana/mes/año) Pensamiento sobre dolor (0-3)	Inicio 6 semanas	Significativa disminución de la intensidad del dolor en el grupo de intervención comparado con el GC (p = 0,024)	Tto. 6 semanas, dos veces/semana

			física	Escala de depresión de Beck Calidad de vida Escala de imagen corporal			
Castien et al [36]	82	Edad: 40 años Hombre/Mujer: 9/32 CTC Duración: 13 años	Movilizaciones y ejercicio craneocervical (n = 41) GC: información, avisos y medicación (analgésicos y antiinflamatorios no esteroideos) (n = 41)	Frecuencia (días/mes) Número de migrañas/mes Intensidad de la NRS (0-10) Test de impacto de las cefaleas (36-78) Inventario de discapacidad en cefaleas (0-100) Rango cervical de movimiento (grados) Algometría (0-80 puntos) Test de resistencia de los flexores del cuello (s) Ausencia laboral y visitas al médico (días)	Inicio 8 semanas 26 semanas	Hubo diferencias significativas entre grupos a favor del grupo de intervención en frecuencia, intensidad del dolor e impacto de la cefalea en el paciente. La terapia manual junto con el ejercicio proporciona una efectiva intervención en pacientes con CTC	ITT Algunas variables se analizaron con tests no paramétricos al no seguir una distribución normal Tto. de 30 min

Torelli et al [35]	48	Edad: 40 años Hombre/Mujer: 15/33 CTC y episódica Duración: 45 años	Fisioterapia y ejercicio para cuello, hombros y cráneo (n = 41) GC: observación 8 semanas y luego mismo tratamiento que el grupo anterior	Frecuencia (días/mes) Intensidad del dolor (0-3) Duración (h/día) Consumo de medicación (n.º de dosis)	Inicio 8 semanas 16 semanas 20 semanas 28 semanas (sólo GC)	El número de días con cefalea disminuyó de forma significativa en ambos grupos tras el tto. de fisioterapia. El consumo de medicación disminuyó significativamente en ambos grupos después del seguimiento frente a la línea base. Mujeres con CTC respondieron mejor. Durante el período de observación no se vieron cambios	Tto. de dos veces a la semana durante 4 semanas Sesgos en GC

Tabla I. Características epidemiológicas de los estudios y resultados y conclusiones de cada uno de ellos. CTC: cefalea tensional crónica; ECC: entrenamiento craneocervical; EVA: escala visual analógica; GC: grupo control; ITT: análisis por intención de tratar; NRS: escala numérica de dolor; tto.: tratamiento.

– *Resultados de la valoración de la calidad metodológica utilizando la escala Delphi.*

Tras la valoración de la calidad metodológica de los estudios con la escala Delphi, se obtuvo como resultado que siete de los ECA mostraron una calidad metodológica aceptable con puntuaciones de 6 o más(Castien et al., 2011; De Hertogh et al., 2009; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Torelli et al., 2004; van Ettekoven & Lucas, 2006; Varkey et al., 2011); los otros tres estudios obtuvieron una puntuación de 5 o inferior, considerándose que presentan una calidad deficiente(27–29). La puntuación media total de calidad metodológica fue de 6,0 con una desviación típica de 1,6 con rango de entre 3 y 8 puntos.

Fue necesaria la intervención de un tercer evaluador independiente para obtener un consenso en la evaluación de tres de los estudios(John et al., 2007; F Mongini et al., 2012; van Ettekoven & Lucas, 2006), la concordancia entre los evaluadores según el coeficiente de kappa fue alta 0,87.

En la ***Tabla II*** se presentan los resultados numéricos de la escala Delphi.

	ITEM 1	**ITEM 2**	**ITEM 3**	**ITEM 4**	**ITEM 5**	**ITEM 6**	**ITEM 7**	**ITEM 8**	**ITEM 9**	**ITEM 10**	**Total**
Soderberg et al [32]	1	1	1	1	0	0	0	0	1	1	6
Soderberg et al [31]	1	1	1	1	0	0	0	1	1	1	7
Van Ettekoven et al [33]	1	0	1	1	1	0	0	1	1	0	6
Mongini et al [30]	1	0	1	0	0	0	0	1	0	1	4
John et al [29]	1	0	1	1	0	0	0	1	0	1	5
De Hertogh et al [27]	1	1	1	1	1	0	0	1	0	1	7
Varkey et al [34]	1	1	1	1	1	0	0	1	1	1	8
Dittrich et al [28]	1	0	1	0	0	0	0	1	0	0	3
Castien et al [36]	1	1	1	1	1	0	0	1	1	1	8
Torelli et al [35]	1	0	1	1	0	1	0	1	0	1	6

Tabla II. Puntuación ensayos clínicos aleatorizados con la escala Delphi

1: se realizó una distribución aleatoria; 2: existió una adecuada ocultación de la asignación; 3: los grupos de estudio eran similares; 4: se especificaron los criterios de elección; 5: se cegó al que valoró el resultado; 6: se cegó al que realizó el tratamiento; 7: se cegó al paciente; 8: se presentan las estimaciones de los resultados y las medidas de variabilidad; 9: análisis por intención de tratar; 10: índice de retiro y abandonos.

- *Características de la población de los estudios*

Todos los estudios fueron realizados en población con migrañas y/o CTT según la ICHD y entre cada una de las muestras, las CTT fueron las que presentaron mayor cantidad de casos. Cabe destacar que sólo uno de los estudios incluyó a pacientes, en parte de su muestra, con otro tipo de cefalea distinta a la CTT o a la migraña(De Hertogh et al., 2009).

Todos los estudios, a excepción de uno(Dittrich et al., 2008), describieron pérdidas y abandonos de sus pacientes durante el tiempo de la intervención y el proceso de análisis y cinco estudios describieron que se realizó el análisis por intención a tratar(Castien et al., 2011; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; van Ettekoven & Lucas, 2006; Varkey et al., 2011).

Se evaluó un total de 2495 pacientes y la media de edad de los pacientes fue de 41,65 años con un rango de edad (obtenido de la edad media) entre 33 y 47 años. El 77% de la muestra fueron mujeres y el 23% hombres.

Sólo uno de los ensayos describe la localización del dolor(De Hertogh et al., 2009) y en otros tres(E. I. Soderberg et al., 2011; Torelli et al., 2004; Varkey et al., 2011) se ha registrado el tiempo en años desde que los pacientes tenían dolor de cabeza. Dos estudios valoraron el nivel académico(F Mongini et al., 2012; E. I. Soderberg et al., 2011). La duración del dolor en horas fue también registrada por cuatro de los ocho estudios valorados(Castien et al., 2011; John et al., 2007; Torelli et al., 2004; van Ettekoven & Lucas, 2006). Además en cinco ensayos(John et al., 2007; F Mongini et al., 2012; Torelli et al., 2004; van Ettekoven & Lucas, 2006; Varkey et al., 2011) se recogió el consumo de medicación en dosis semanales expresadas en días. Por último, las variables más comunes fueron la intensidad del dolor medida en distintas escalas: de 0-5(Dittrich et al., 2008; F Mongini et al., 2012), escala de 0-10(Castien et al., 2011;

John et al., 2007; van Ettekoven & Lucas, 2006) y escala de 0-100(De Hertogh et al., 2009; E. Soderberg et al., 2006; Varkey et al., 2011) y la frecuencia de los ataques (medida en días al mes)(Castien et al., 2011; De Hertogh et al., 2009; Dittrich et al., 2008; John et al., 2007; F Mongini et al., 2012; Torelli et al., 2004; van Ettekoven & Lucas, 2006; Varkey et al., 2011). Otras características de las poblaciones de los estudios se pueden observar en la Tabla I.

- *Características de la intervención*

La mayor parte de los estudios han tenido un seguimiento de 6 meses(Castien et al., 2011; F Mongini et al., 2012; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Torelli et al., 2004; van Ettekoven & Lucas, 2006; Varkey et al., 2011) y todos excepto uno(Dittrich et al., 2008) han tenido como mínimo 3 meses de seguimiento. La utilización de diversas técnicas de ET en la intervención asignada en los grupos experimentales es una de las características en la que todos los estudios coinciden. Además, siete de los ECA han prescrito tratamientos para realizar en casa(Castien et al., 2011; F Mongini et al., 2012; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Torelli et al., 2004; van Ettekoven & Lucas, 2006; Varkey et al., 2011). Tres de los ensayos han incluido una terapia de ejercicios específicos cráneo-cervicales(Castien et al., 2011; De Hertogh et al., 2009; van Ettekoven & Lucas, 2006). Siete artículos incluyeron un Grupo Control (GC)(Castien et al., 2011; De Hertogh et al., 2009; Dittrich et al., 2008; John et al., 2007; F Mongini et al., 2012; Torelli et al., 2004; van Ettekoven & Lucas, 2006) y los otros tres realizaron una comparación de tres técnicas diferentes (Soderberg et al., 2006; Soderberg et al., 2011; Varkey et al., 2011) tales como la relajación, acupuntura o tratamiento farmacológico (Topiramato). Dentro de los GC, las actuaciones que se realizaron fueron: tratamiento convencional de fisioterapia, corrección postural, auto-administración de un programa de ejercicios, educación para domicilio, auto-cuidados, o tratamiento médico convencional. Resulta importante destacar que tres ensayos(Castien et al., 2011; De Hertogh et al., 2009; van Ettekoven & Lucas, 2006) utilizaron el mismo protocolo de ejercicio terapéutico descrito por Jull y cols. en 1997.

Debe tenerse en cuenta que casi todos los pacientes mantienen el tratamiento farmacológico de base consistente en analgésicos comunes sin tratamiento específico.
Podemos dividir las intervenciones en dos grupos diferenciados (ejercicio terapéutico dirigido a la región cráneo-cervical por un lado y ejercicio activo general por otro) cuyas características se describen a continuación.

- *Intervenciones*

  Ejercicio terapéutico cráneo-cervical (ETCC)(Castien et al., 2011; De Hertogh et al., 2009; van Ettekoven & Lucas, 2006)

Todos los ejercicios se realizaron bajo supervisión de Fisioterapeutas experimentados. La duración de las sesiones de tratamiento osciló entre 15-30 min. 2 veces a la semana y un máximo de 9 a 12 sesiones. Los tratamientos se prolongaron entre 6 y 8 semanas.

Para el ejercicio terapéutico cráneo-cervical, realizaron ejercicios de baja carga de resistencia para los músculos flexores profundos del cuello(Castien et al., 2011; De Hertogh et al., 2009; van Ettekoven & Lucas, 2006). Estos ejercicios específicos de baja carga se combinaron con otras técnicas como la movilizaciones articulares(De Hertogh et al., 2009; van Ettekoven & Lucas, 2006), correcciones posturales(Castien et al., 2011; van Ettekoven & Lucas, 2006) o ejercicios domiciliarios(Castien et al., 2011; van Ettekoven & Lucas, 2006).

Algunos ejercicios dirigidos a la región cráneo-cervical se realizaron utilizando una banda de látex (Thera-Band®)(van Ettekoven & Lucas, 2006) para hacer frente a las deficiencias en las sinergias de los músculos flexores del cuello que se observaron en pacientes con cefaleas de origen cervical y otros trastornos de dolor de cuello(Bendtsen, 2003; Watson & Trott, 1993). La resistencia de la banda fue utilizada de tal manera que se ejercitaran los músculos profundos del cuello(Mayoux-Benhamou et al., 1994).
Los participantes fueron instruidos para llevar a cabo una flexión cráneo-cervical lenta y controlada sobre diferentes gamas de movimiento.

La duración de las sesiones de tratamiento del ETCC no excedió de 30 min.

Ejercicio activo no dirigido (EA)(Dittrich et al., 2008; John et al., 2007; Mongini et al., 2012; Soderberg et al., 2006; Soderberg et al., 2011; Torelli et al., 2004; Varkey et al., 2011).

La mayor parte de los ejercicios fueron coordinados y diseñados por fisioterapeutas cualificados(E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Torelli et al., 2004; Varkey et al., 2011). Otro programa fue diseñado por un médico y sus colaboradores(F Mongini et al., 2012). En otro ensayo, los ejercicios fueros controlados por un terapeuta de yoga(John et al., 2007), y por último, uno de los estudios no detalla quién dirigía el programa de ejercicios(Dittrich et al., 2008).

La duración de los EA fue entre 45-60 min. de 6 a 12 semanas y con un periodo de ejercicios post-tratamiento de hasta 4 semanas.

Estos EA incluyeron sesiones de fortalecimiento en clínica para el cuello y hombros, instrucciones sobre cómo reducir la parafunción y la hiperfunción de la los músculos cráneo-faciales y el cuello durante el día, estiramientos musculares, ejercicios de relajación y ejercicios respiratorios(John et al., 2007; F Mongini et al., 2012; Torelli et al., 2004). Adicionalmente, todas las formas de ejercicio aeróbico continuo (por ejemplo bicicleta estática) fueron aceptadas como ejercicio terapéutico para formar parte de este grupo(Dittrich et al., 2008; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Varkey et al., 2011).

Algunos de los pacientes recibieron una demostración práctica y además se les proporcionó una hoja escrita con ilustraciones de los ejercicios y las instrucciones. Los participantes también tuvieron acceso a un sitio Web para ver un vídeo de demostración(F Mongini et al., 2012).

Algunos de estos programas de ejercicios han sido descritos con anterioridad(Varkey, Cider, Carlsson, & Linde, 2009).

- *Análisis Cualitativo*

A continuación describimos el análisis cualitativo de los resultados según el nivel de evidencia. En este apartado únicamente hemos podido agrupar los estudios que presentaron una homogeneidad clínica y metodológica entre sí.

- Existe evidencia moderada (3 estudios(Castien et al., 2011; Torelli et al., 2004; van Ettekoven & Lucas, 2006); n=211 pacientes) que demuestra que un tratamiento de fisioterapia que incluye ejercicio terapéutico enfocado a la reeducación y re-entrenamiento de la musculatura cráneo-cervical y del hombro mejora significativamente a medio plazo la frecuencia, la intensidad y duración del dolor, así como el nivel de discapacidad en pacientes que presentan CTT.
- Existe evidencia limitada (2 estudios(Dittrich et al., 2008; Varkey et al., 2011); n=121) que demuestra que el ejercicio terapéutico de carácter aeróbico muestra efectos positivos sobre pacientes que presentan migraña, sin embargo esta intervención no es superior a otros tratamientos.
- Existe diferencia fuerte (7 estudios(Castien et al., 2011; De Hertogh et al., 2009; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Torelli et al., 2004; van Ettekoven & Lucas, 2006; Varkey et al., 2011); n=519) que demuestra que diversas modalidades de ejercicio terapéutico no producen efectos adversos sobre pacientes que presenten CTT o Migrañas.

4. DISCUSIÓN

El análisis realizado en esta revisión, basado en los resultados y conclusiones de los estudios seleccionados, describe efectos positivos del ejercicio terapéutico prescrito de manera individual o combinado con otra intervención de fisioterapia o educación. De los diez estudios seleccionados, siete presentaron una buena calidad metodológica obteniendo 6 o más puntos en la escala Delphi(Castien et al., 2011; De Hertogh et al., 2009; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Torelli et al., 2004; van Ettekoven & Lucas, 2006; Varkey et al., 2011).

El análisis de los resultados muestra que en la mayoría de los estudios se describió una disminución significativa de los síntomas asociados a esta dolencia como son la intensidad del dolor, la frecuencia o la discapacidad, cuando se comparan con la

situación previa del paciente(De Hertogh et al., 2009; F Mongini et al., 2012; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Varkey et al., 2011). Sin embargo hay que destacar que en cuatro de ellos, el ejercicio terapéutico, resultó superior a otras intervenciones como la corrección postural combinada con fisioterapia convencional, educación sobre los efectos del ejercicio o un programa médico que combina información, avisos para mejorar el estilo de vida y medicación contra el dolor (Castien et al., 2011; Dittrich et al., 2008; John et al., 2007; van Ettekoven & Lucas, 2006).

Revisiones sistemáticas previas han obtenido resultados similares a esta, en relación con esto, Bronfort y cols(G Bronfort et al., 2004) describieron que diferentes tratamientos de fisioterapia presentaban efectos positivos sobre pacientes con cefaleas crónicas de diverso tipo. En otras revisiones también se observaron efectos positivos del ejercicio terapéutico sobre pacientes con cefaleas(Busch & Gaul, 2008; Fricton, Velly, Ouyang, & Look, 2009), sin embargo, las limitaciones metodológicas que presentan los estudios analizados impiden que se puedan formular conclusiones relevantes.

Uno de las aspectos importantes a destacar es que ninguno de los estudios analizados describió efectos adversos tras la realización del ejercicio terapéutico combinado o no con fisioterapia manual, incluso en uno de los estudios se ha propuesto como tratamiento preventivo para las migrañas en aquellos pacientes que no deseen ingerir medicación(Varkey et al., 2011). En esta línea, otro de los artículos, con alta calidad metodológica y con un tamaño del efecto elevado, demostró ser superior a la ingesta de medicación (analgésicos y AINES)(Castien et al., 2011). Estos datos resultan relevantes teniendo en cuenta los efectos adversos que se pueden producir y que han sido cuantificados por las intervenciones farmacológicas realizadas en pacientes con cefaleas(Pini, Bigarelli, Vitale, & Sternieri, 1996).

A pesar de que los resultados de los ensayos clínicos muestran efectos positivos del ejercicio terapéutico sobre pacientes con migrañas y CTT, estos deben analizarse con precaución ya que 4 de los 10 estudios analizados presentan una baja calidad metodológica. Por lo tanto, se debe tener en cuenta que la interpretación de los resultados de una revisión sistemática no depende únicamente de los resultados

obtenidos en los estudios analizados, sino que es fundamental la calidad metodológica de los mismos para elaborar conclusiones que presenten mayor validez científica y clínica (Juni, Altman, & Egger, 2001; Verhagen, de Vet, de Bie, Boers, & van den Brandt, 2001). Es por esta razón, por la que se ha decido describir los resultados según el análisis cualitativo basado en los niveles de evidencia científica, destacando que estos se estructuran basándose en la calidad metodológica y en la homogeneidad clínica de los estudios analizados(van Tulder et al., 2003). Consideramos que los 4 estudios analizados(Castien et al., 2011; De Hertogh et al., 2009; Torelli et al., 2004; van Ettekoven & Lucas, 2006) donde se aplican métodos de fisioterapia incluyendo ejercicio terapéutico para pacientes con CTT son clínicamente relevantes teniendo en cuenta los efectos positivos descritos frente a la intervención del grupo control y sobre todo, que los 4 estudios presentan una buena calidad metodológica(Castien et al., 2011; De Hertogh et al., 2009; Torelli et al., 2004; van Ettekoven & Lucas, 2006). Con respecto a los otros estudios que presentaron una buena calidad metodológica cabe decir que ha sido difícil agruparlos en un solo resultado ya que presentaron características muy heterogéneas en cuanto a criterios clínicos y metodológicos.

En cuanto a las características de la intervención cabe destacar que en 2 de los estudios(Dittrich et al., 2008; E. Soderberg et al., 2006; E. I. Soderberg et al., 2011; Varkey et al., 2011) el ejercicio terapéutico que se prescribió fue de tipo aeróbico y en los otros ocho(Castien et al., 2011; De Hertogh et al., 2009; John et al., 2007; F Mongini et al., 2012; Torelli et al., 2004; van Ettekoven & Lucas, 2006) se han prescrito ejercicios enfocados al re-entrenamiento y re-educación de regiones anatómicas del hombro y el cuello. Este planteamiento clínico-metodológico se justifica teniendo en cuenta que los síntomas de dolor de cuello y hombro presentan una gran comorbilidad con las cefaleas primarias, principalmente con las migrañas y las CTT(Blaschek et al., 2012; A H Calhoun et al., 2010; Grimmer, Nyland, & Milanese, 2006; Watson & Drummond, 2012). Algunos autores han relacionado el dolor de cuello con la hiperalgesia bilateral del área trigeminal(R La Touche et al., 2010) a través de la relación somatosensorial que se genera por la convergencia de información sensorial de las neuronas de segundo orden del nervio trigémino y de los tres primeros niveles espinales en el núcleo trigémino cervical(Bogduk & Govind, 2009). Por otro parte, Jull

y cols observaron la efectividad del ejercicio terapéutico dirigido a los flexores profundos del cuello, músculos que son inervados por las primeras raíces espinales, en pacientes que presentaron cefaleas secundarias de origen cervical(Jull et al., 2002).

Sugerimos que el ejercicio terapéutico debe considerarse como parte integral de un abordaje biopsicosocial de pacientes que sufran migrañas y CTT. Los resultados analizados de la evidencia actual nos llevan a teorizar a que el ejercicio terapéutico puede prescribirse para disminuir los síntomas músculo-esqueléticos de hombro, cuello y cabeza asociados a este tipo de cefaleas. Por otra parte, consideramos que el ejercicio terapéutico cumple un objetivo muy importante en cuanto al proceso de aprendizaje intrínseco de este tipo de tratamiento que su vez puede ayudar a que el paciente genere habilidades de afrontamiento activo necesario para disminuir los síntomas y mejorar la autoeficacia percibida frente a su dolencia. La investigación relacionada con los efectos del ejercicio terapéutico sobre las cefaleas primarias ha mostrado principal interés sobre las migrañas y las CTT y así lo demuestra esta revisión, esto podría deberse a que el resto de cefaleas primarias epidemiológicamente no presentan síntomas y signos musculo-esqueléticos tan prevalentes como las migrañas y las CTT.

Es importante destacar que ha resultado imposible realizar un meta-análisis debido a que en un gran número de los estudios no se presentaban los datos estadísticos de forma clara o con el formato necesario para ser meta-analizados. Otro factor a tener en cuenta es la gran heterogeneidad de las variables de medición utilizadas. Finalmente, una dificultad añadida ha sido la baja calidad metodológica de algunos de los artículos seleccionados para esta revisión, y se recomienda que un meta-análisis incluya únicamente ECA de buena calidad metodológica.

CHAPTER 3. Effectiveness of Therapeutic Patient Education for Adults with Migraine. A Systematic Review and Meta-Analysis of Randomized Controlled Trials

1. INTRODUCTION

Biobehavioral treatments (BBTs) for chronic pain patients includes therapeutic patient education (TPE) and selfcare, cognitive behavioral interventions, and biobehavioral training (biofeedback, relaxation training, and stress management) (Frank Andrasik et al., 2009; Carlson, 2008; Rains et al., 2005) BBT helps the patient change the way they think about their condition, as well as make changes in maladaptive pain behaviors to healthy behaviors. The treatments are designed to help patients to manage their symptoms and their lives (Sluka & Turk, 2009).

TPE provides contact between the care providers and patients (Daviet et al., 2012) to allow patients to become autonomous in the long term by offering the psycho-pedagogic means that are essential to motivate patients to treat themselves (Reed, 2010).

1. TPE has been extensively studied in the management of anxiety, stress, and pain for chronic lower back pain (Louw, Diener, Butler, & Puentedura, 2011b). It is thought that in chronic diseases, TPE should be adapted to the needs of patients and caregivers (Daviet et al., 2012).

The purpose of this systematic review and meta-analysis was to conduct a current review of randomized controlled trials (RCTs) concerning the effectiveness of TPE on pain, disability, and psychological outcome among patients with migraine.

2. METHODS

The systematic review was performed using a predefined protocol and subdivided into phases based on rules of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009).

2.1. Participants

– *Inclusion Criteria of the Studies*

The selection criteria used in this review were based on methodological and clinical aspects such as the type of study, study population, interventions, and outcome measures.

– *Type of Studies*

We selected RCTs to compare with a control group or other interventions that were methodologically correct. Only studies published in English and Spanish were included. The systematic review was performed using a predefined protocol and subdivided into phases based on rules of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009).

– *Inclusion Criteria of the Studies*

The selection criteria used in this review were based on methodological and clinical aspects such as the type of study, study population, interventions, and outcome measures.

– *Patients*

The patients of the trials selected had to be over 18 years, diagnosed with migraine or chronic migraine according to the IHS classification.

2.2. Variables and Instruments

– *Therapeutic Intervention*

RCTs that were included were based on a TPE approach, with major interventions based on the patients' learning and coping strategies.

– *Measures of Success*

The measures that check the results and effects of the treatment had to assess at least two or more of the related variables: pain intensity, frequency of headache, disability, quality of life, depression symptoms, and self-efficacy. Furthermore, these had to be registered in the short term (<3 months), intermediate term (between 3 months and 12 months), or long term (>12 months).

2.3. Procedure

– *Search Strategy*

The search of scientific articles was performed using MEDLINE (1950 to May 2013), EMBASE (1988 to May 2013), PEDro (1999 to May 2013), CINAHL (1982 to May 2013), and PsychINFO (1806 to May 2013), with May 15, 2013, being the final date of the search. The terms used for the search were derived from the combination of the following words: "patient education," "patient informa-tion," "behavioral therapy," "behavioral treatment," "cogni-tive treatment," "information booklet," "educational booklet," "educational intervention," "advice," "coping strategies," "web-based intervention," "web-based edu-cation," "headache intensity," "quality of life," "headache frequency," "randomized controlled trial," and "migraine." The search strategy was adapted for each database as necessary. Two independent reviewers conducted the search using the same method, and any differences that emerged in this phase were resolved by consensus.

– *Selection Criteria and Data Extraction*

The first analysis of the data was performed by two inde-pendent reviewers who assessed the RCTs' relevance regarding the studies' questions and objectives. This first analysis was performed based on information from the title, abstract, and keywords of

each study. If there was no consensus, or the abstracts did not contain sufficient information, the full text was reviewed.

In the second phase of the analysis, using the full text, we proceeded to test whether the studies met all of the inclusion criteria. Differences between reviewers were resolved by a process of discussion/consensus moder-ated by a third reviewer (Furlan et al., 2009). Data described in the results were extracted by means of a structured protocol that ensured the most relevant information from each study was obtained (Higgins JPT, 2011).

– *Methodological Quality Assessment*

The assessment of the methodological quality of the studies was performed using the Delphi list (Verhagen et al., 1998). This instrument was developed through a consensus of experts who established 10 items: 1) randomization per-formed; 2) random allocation concealed; 3) study groups similar at baseline; 4) inclusion and exclusion criteria specified; 5) outcome assessor blinded; 6) care provider blinded; 7) patient blinded; 8) estimates and measures of variability presented for primary outcomes; 9) intention-to-treat analysis; and 10) index of withdrawals and dropouts described.

Methodological criteria were scored as: yes (one point), no (zero points), or don't know (zero points). The maximum possible score was 10, with a range of 0–10. Studies were considered to be of high quality when they met six or more items (van Tulder et al., 2003). The Delphi list showed good concurrent validity with the Jadad scale (Spearman r = 0.63–0.71) and inter-rater reliability between 0.54 and 0.85 (Olivo et al., 2008).

Two independent reviewers examined the quality of all of the studies selected using the same methods, and dis-agreements between reviewers were resolved by consen-sus including a third reviewer. The inter-rater reliability was determined using the Kappa coefficient, where >0.7 indi-cated a high level of agreement between assessors, between 0.5 and 0.7 indicated a moderate level of agree-ment, and <0.5 indicated a low level of agreement (Cohen, 1960).

– *Classification of Evidence Levels*

The qualitative analysis used was based on the classifica-tion of the results in evidence levels (van Tulder et al., 2003). Evidence was categorized into five levels depending on the methodologi-cal quality as follows: 1) strong evidence: consistent among multiple high-quality RCTs; 2) moderate evidence: consistent findings among multiple low-quality RCTs, and/or clinical controlled trials (CCTs), and/or one high-quality RCT; 3) limited evidence: one low-quality RCT and/or CCT; 4) conflicting evidence: inconsistent findings among multiple trials (RCTs and/or CCTs); and 5) no evidence: no RCTs or CCTs.

– *Data Synthesis and Analysis*

Statistical analysis was conducted using Meta-analysis with Interactive Explanations (MIX, version 1.7, BiostatXL, Mountain View, CA, USA) (Bax, Yu, Ikeda, Tsuruta, & Moons, 2006). The meta-analysis was performed in accordance with the PRISMA guidelines (David Moher et al., 2009).

The same inclusion criteria were used for the systematic review, as well as for the meta-analysis, and included three more criteria: 1) in the results, there was detailed informa-tion regarding the comparative statistical data of the expo-sure factors, therapeutic interventions, and treatment responses; 2) the TPE treatment was compared with a control group or another treatment; and 3) data of the analyzed variables were represented in at least two studies.

To provide a comparison between outcomes reported by the studies, the standardized mean difference (SMD) over time and corresponding 95% confidence interval (CI) were calculated for continuous variables and, if possible, short-term, intermediate-term, and long-term follow-up time points. The statistical significance of the pooled SMD was examined by a Z-test.

The effect estimates SMDs were interpreted as described by Hopkins et al. (Hopkins, Marshall, Batterham, & Hanin, 2009). SMD of 4.0 was rep-resented an extremely large clinical effect, 2.0–4.0 rep-resented a very large effect, 1.2–2.0 represented a large

effect, 0.6–1.2 represented a moderate effect, 0.2–0.6 represented a small effect, and 0.0–0.2 represented a trivial effect.

To compare the data, the following statistical tests were performed: the DerSimonian-Laird Q-test to measure the level of heterogeneity, and publication bias was also examined with Egger's regression tests (Begg & Mazumdar, 1994). When the Q-test was significant ($P < 0.05$), this indicated that heterogeneity existed among the studies, and the random effects model was conducted in the meta-analysis.

3. RESULTS

– *Study Selection*

As shown in **Figure 1**, a total of 89 studies were identified. Of these, 57 were dismissed because after reviewing the abstracts, it was concluded that these papers did not meet the inclusion criteria. Eighteen studies were with-drawn because six of them were not RCTs, two of them did not mention the population age, two not TPE treat-ment, five trials did not include patients diagnosed for specific migraine, and three studies included multiple pathologies. Fourteen studies (Bromberg et al., 2012; Cady et al., 2009; Anne H Calhoun & Ford, 2007; Günther Fritsche et al., 2010; Hedborg & Muhr, 2011, 2012; K A Holroyd et al., 1989; Kenneth A Holroyd et al., 2010; Lemstra, Stewart, & Olszynski, 2002; Matchar et al., 2008; Saskia Y.M. Mérelle, Sorbi, van Doornen, & Passchier, 2008; S Y M Mérelle, Sorbi, van Doornen, & Passchier, 2008; Rothrock et al., 2006; Seng & Holroyd, 2010), all of them RCTs, met the inclusion criteria and were included in the system-atic review. Only nine (Bromberg et al., 2012; Günther Fritsche et al., 2010; Hedborg & Muhr, 2011; Lemstra et al., 2002; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008; Seng & Holroyd, 2010) of the 14 studies were chosen for further analysis by including them in the meta-analysis.

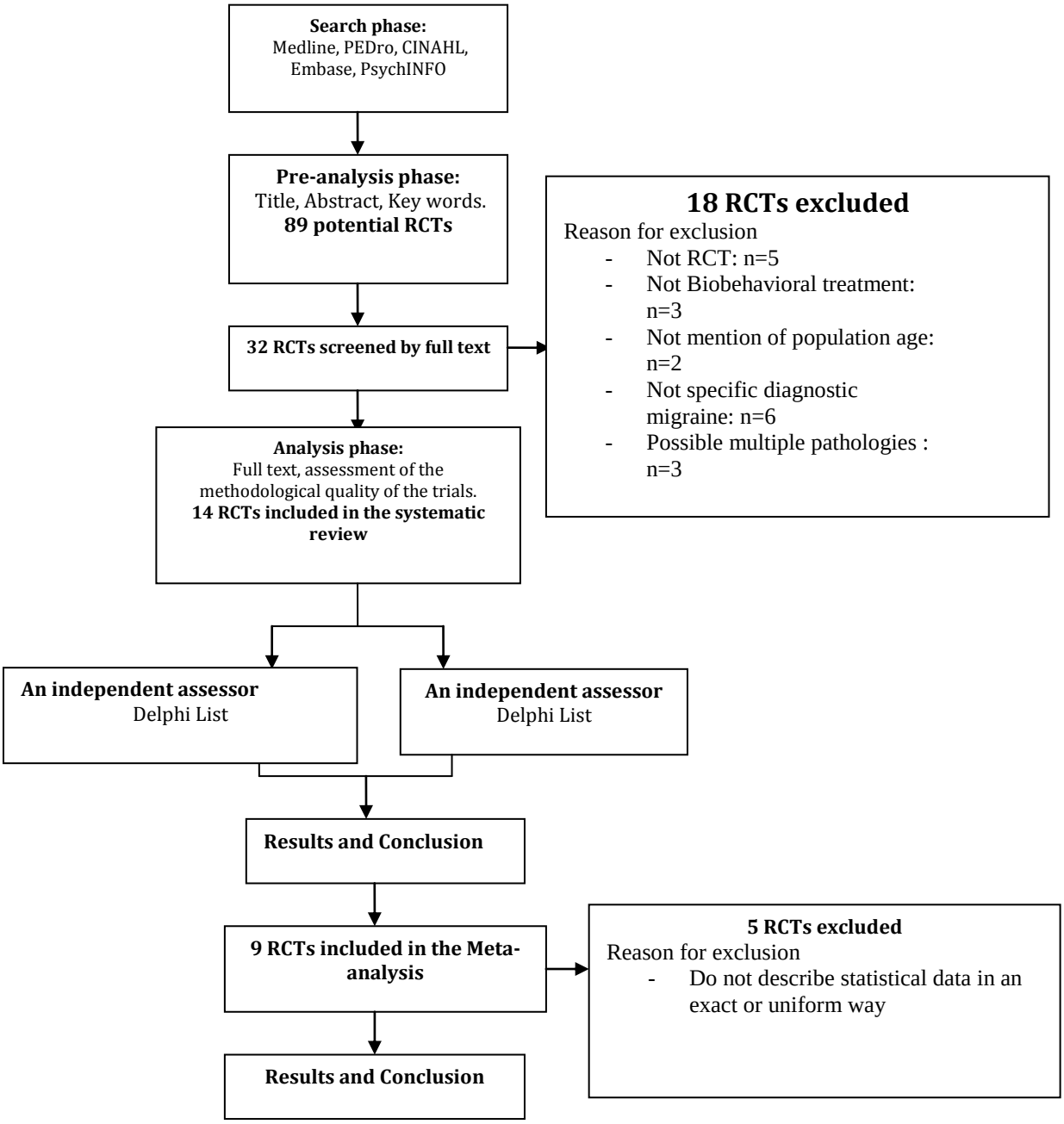


Figure 1. Flow chart of the selection of clinical trials

– *Methodological Quality Analysis*

The trials were evaluated with the Delphi list scale revealed a median score of 6.14 ± 1.29 (range: 5–9). According to the analyses of two reviews, eight (Bromberg et al., 2012; Cady et al., 2009; Hedborg & Muhr, 2011; Kenneth A Holroyd et al., 2010; Lemstra et al., 2002; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008; S Y M

Mérelle et al., 2008) of the studies' methodologies were acceptable in terms of quality, but the other six (Anne H Calhoun & Ford, 2007; Günther Fritsche et al., 2010; Hedborg & Muhr, 2012; K A Holroyd et al., 1989; Rothrock et al., 2006; Seng & Holroyd, 2010) were consid-ered poor quality. **Table 1** shows the results of the evaluation according to the Delphi list scale.

The two reviewers had discrepancy in the evaluation of two RCTs. The discrepancy for those two studies con-cerned their scores for items 2 and 6. A consensus was reached after the third reviewer intervened. The inter-rater reliability of the methodological quality assessment was high ($\kappa = 0.93$, 95% CI 0.90–0.95).

Most of the studies lacked assessor, care provider, and blinding of the patients.

– *Study Characteristics*

The characteristics (sample size, intervention, follow-up period, and main results) of the data were extracted and are presented in Table 2.

– *Characteristics of TPE in Patients with Migraine*

Two studies (14.28%) (Bromberg et al., 2012; Hedborg & Muhr, 2012) used Internet in their behavioral treatments, employing a multimodal behavioral treatment via Internet (Hedborg & Muhr, 2011) or a web BBT. They also included diet educational approach (Hedborg & Muhr, 2012). Three studies (21.42%) (Kenneth A Holroyd et al., 2010; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008) educated the patients in a biobehavioral approach based on relaxation.

	ITEM Nº:										
TRIAL	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**TOTAL**
Rothrock J (2006)	1	1	1	0	0	0	0	1	0	1	5
Matchar D (2008)	1	1	1	1	0	0	0	1	0	1	6*
Fritscher G (2010)	1	0	1	1	0	0	0	1	0	1	5
Cady R (2009)	1	1	1	1	1	0	1	1	1	1	9*

Hedborg H (2011)	1	1	1	1	0	0	0	1	1	1	7*
Merelle S (2007)	1	1	0	1	1	1	0	1	1	1	8*
Merelle S (2008)	1	0	1	1	0	0	0	1	1	1	6*
Bromberg J (2012)	1	1	1	1	0	0	0	0	1	1	6*
Lemstra M (2002)	1	1	1	1	1	0	0	1	1	1	7*
Seng E (2010)	1	0	0	0	0	1	1	1	0	1	5
Holroyd K (2010)	1	1	1	1	0	1	1	0	0	1	7*
Calhoun A (2007)	1	1	1	1	0	0	0	0	0	1	5
Holroyd K (1989)	1	0	1	1	0	1	0	0	0	1	5
Hedborg H (2012)	1	0	1	1	0	0	0	1	0	1	5

Table 1. Methodological quality of the studies included in the systematic review (Delphi List scores): (1) Was a method of randomization performed?, (2)Was the treatment allocation performed?, (3) Were the groups similar at baseline?, (4) Were the elegibility criteria specified?, (5) Was the outcome assessor blinded?, (6) Was the care provided blinded?, (7) Was the patient blinded?, (8) were point estimates and measures of variability presented for the primary outcome measures?, (9) Did the analysis include an intention-to-treat analysis? , (10) Is the Withdrawal/drop out rate described?
*Studies that have an acceptable quality.

STUDIES	Patients	Format of education	Education/ biobehavioral Intervention (EI)	Control Intervention (CI)	Outcome measures	Follow-up	Main results
Matchar et al .2008	*N= 614*	1.Informative class (headache types/triggers/ treatment options) 2.Diagnosis and treatment by a professional 3.Proactive follow-up by a care manager	Behavioral treatment	Usual care (by primary care provider)	MIDAS H Frecuency SF 36 PHQ-9	6 months 12 months	At 6 months Behavioral treatment showed improvements in MIDAS (P= .008)
Fritscher et al. 2010	*N= 150*	Guided reading containing information about physiological and psychological aspects of migraine	Biblio group	Behavioral minimal contact therapy	H Frequency Overuse drugs Headache disability Depression	1 month 3 months 12 months	Headache days, migraine days, medication intake ;EI=CI Psychological improvements at short and long term
Hedborg K,	*N=83*	Multimodal behavioral	GA. Hand	Placebo	MADRS	5 months	GA, GB> 50% reduction in

et al 2011		treatment (for behavioral modification) via internet	massage + MBT GB. Extended baseline+ MBT	treatment	PQ23 Changes in migraine frequency	8 months 11 months	migraine frequency
Merelle S, et al 2007	*N=129*	Identification and modification of triggers (affective, cognitive and behavioral) psychological self-regulation skills/ relaxation	Behavioral treatment	Waitlist control	H. frequency SF-36 (m, p) HSE HLS MIDAS	Pre intervention Post intervention	EI Patients with high attack frequency showed better improvements (p=0.03)
Merelle S, et al 2008	*N=127*	Identification and modification of triggers (affective, cognitive and behavioral) psychological self-regulation skills/	Behavioral treatment	Waitlist control	H frequency SF-36 (m, p) HSE HLS MIDAS	6 months	H frequency decreased in EI at 6 months Quality of life improve overtime

		relaxation					
Bromberg J, et al 2012	*N=185*	Migraine specific knowledge/ migraine self management skills/ emotional coping/ communication skills/ medication safety	Behavioral treatment	Control group	HSE HSLCIn MIDAS Depression	3 months 6 months	EI greater than CI in; H self-efficacy, social support, relaxation, pain catastrophizing, depression and stress
Lemstra M, et al 2002	*N= 80*	Exercise therapy lectures/ dietary lecture/ massage therapy	Behavioral treatment	Control group	H frequency Beck Pain disability	3 months	EI better than CI in H frequency, Beck and Pain disability
Seng E, et al 2010	*N= 176*	Migraine management workbook/ audiotape lessons/ guided home practice of behavioral migraine management skills	OAT+ PLACEBO+ BMM OAT+ β blocker+ BMM	OAT+ PLACEBO OAT+ β blocker	HSE HSLC (in, ex) Quality of life	5 months 16 months	EI large increases than CI in HSE and HSCLin and large decreases in HSCLex

Holroyd K, et al 2010	*N=232*	Pathophysiology, migraine management skills, muscle relaxation, migraine triggers and prodromal signs, techniques into patient daily routine, stress management, and thermal biofeedback	OAT+ PLACEBO+ BMM OAT+ β blocker+ BMM	OAT+ PLACEBO OAT+ β blocker	H frequency MSQL	10 months 16 monts	Combined β blocker and behavioral migraine management may improve outcomes in the treatment of frequent migraine
Calhoun A, et al 2007	*N= 43*	Behavioral sleep modifications (8 h in bed, eliminate television, reading and music in bed, visualization technique, move supper and limit fluids, discontinue naps	BSM group	Placebo group	Headache Index H frequency	Pre intervention Post intervention	EI reported statistically significant reduction in headache frequency (p=.01) and headache intensity (p=.01) than CI
Rothrock J ,	*N=100*	Standardized course of	Headache	No school	H frequency	1 month	At 6 months the school group

et al.2006		didactic instruction regarding biogenesis and management	school		H severity MIDAS	3 months 6 months	showed reduction in MIDAS (p<.05)
Cady R, et al.2009	*N= 207*	Patient´s Open-ended question about awareness of migraine symptoms/ Healthcare providing give a list of frequent migraine associated symptoms/ Healthcare provider summarize the information learned by the patient in part 1 and 2	Rizatriptan with M edu Rizatriptan without M edu	Placebo with M edu Placebo without M edu	Hours free of pain	2 hours 24 hours	A greater proportion in the rizatriptan + education group reported pain freedom at 2 hours compared with those in the rizatriptan + no education group
Hedborg K, et al 2012	*N= 76*	Web based, stress Physiology/ physical activity/ Diet/ Tought patterns/Handling of emotions/Attitudes	GA.Hand massage + MBT GB. Extended	Placebo treatment	MADRS PQ23 Changes in migraine frequency	5 months 8 months 11 months	At the end of the MTB, total drug consumption decreased by 22% (p=0.029), corresponding to 27% fewer with migraine headache.

			baseline+ MBT				
Holroyd K, et al 1989	*N= 34*	Identify and monitor signs of headache onset/ develop methods for keeping ergotamine readily available/ adopt an experimental attitude toward decisions about abortive medication/ avoid overuse of medication	SAT+BEI	SAT	Headache Activity/ Medication Use/ Psychological symptoms	Pre intervention Post intervention	Patients in BEI group attempted to abort a greater percentage of their migraine attacks (70% vs 40%) and showed larger reduction in headache activity (e.g., 40% vs 26% reduction in the second month of treatment)

Table 2. Evidence table. Trials (n=14) (identified by first author). H (headache), Riza (Rizatriptan), Pbo (Placebo), w/wout M. Education (With migraine education, without migraine education), G.A (group A), G.B (group B), G.C (group C), MBT (Internet-based multimodal behavior treatment), MADRS-S (Montgomery-Åsberg depression Rating Scale), PQ23 (Quality of life questionnaire), HSLC (Headache Specific Locus of Control Scale), HMSE (Headache Management Self-Efficacy Scale),MSQOL (Quality of life Questionnaire), CPCI-42 (Chronic Pain Coping Inventory -42), HSES (Headache Management Self-efficacy Scale), PSC (Pain Catastrophizing Scale), DASS-21 (Depression Anxiety Stress Scales), PGIC (Patient Global Impression of Change), OAT (Optimized acute treatment), BMM (Behavioral Migraine management), BSM (Behavioral Sleep Modification), SAT (Standard Abortive Therapy), BEI (Brief Educational Intervention).

The medication intake TPE approach was used in two studies (14.28%) (Bromberg et al., 2012; K A Holroyd et al., 1989) that were based on the medica-tion safety described by Bromberg et al. [38] avoiding medication overuse as described by Holroyd et al., (K A Holroyd et al., 1989).

Only one of the included trials (7.14%) used sleep modification and TPE in its biobehavioral approach (Anne H Calhoun & Ford, 2007). Six trials (Cady et al., 2009; Günther Fritsche et al., 2010; Lemstra et al., 2002; Matchar et al., 2008; Rothrock et al., 2006; Seng & Holroyd, 2010) gave the patients an educational approach based on reading guides (14.28%) (Günther Fritsche et al., 2010; Seng & Holroyd, 2010) or lectures, and classes by a professional (28.57%) (Cady et al., 2009; Lemstra et al., 2002; Matchar et al., 2008; Rothrock et al., 2006). The varieties of TPE used in the studies are explained in **Table 2**.

- *Characteristics of Therapies Used in the Control Groups*

Seven RCTs (Bromberg et al., 2012; K A Holroyd et al., 1989; Lemstra et al., 2002; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008; Rothrock et al., 2006) used an usual pharmacological care treatment in the control group applying two of them the current treatment in the waitlist control (Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008). Two of the studies (Kenneth A Holroyd et al., 2010; Seng & Holroyd, 2010) divided the control treatment into two groups, one of them was based on a placebo plus an optimized acute therapy (OAT), and the other was based on medication plus OAT. One trial (Anne H Calhoun & Ford, 2007) used therapy based on placebo plus medication as the control group. Muscular relaxation therapy was used as the control in two RCTs (Hedborg & Muhr, 2011, 2012). One trial subdivided the treatment and placebo groups into patient education or no patient education (Cady et al., 2009). Only one trial designed its control group as a minimal contact education therapy (Günther Fritsche et al., 2010).

- *Systematic Review Results*

Five RCTs (35.7%) evaluated the effects of a TPE and obtained statistically significant results in disability and quality of life by the MIDAS questionnaire (Lemstra et al., 2002; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al.,

2008; Rothrock et al., 2006). Two of them showed positive results at 6 months (Matchar et al., 2008; Rothrock et al., 2006). The headache self-efficacy questionnaire assess self-efficacy about headache outcome in patients and were evaluated in four trials (Bromberg et al., 2012; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008; Seng & Holroyd, 2010) (28.57%). Only one of the studies showed statistically significant results of the self-efficacy at 6 months (Bromberg et al., 2012).

Eight RCTs evaluated headache frequency (57.14%) (Cady et al., 2009; Anne H Calhoun & Ford, 2007; Günther Fritsche et al., 2010; Kenneth A Holroyd et al., 2010; Lemstra et al., 2002; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008) by measuring it at 2 hours after medication (Rizatriptan) intake in one trial (Cady et al., 2009), at 3 and 6 months in two trials, respectively (Lemstra et al., 2002; Matchar et al., 2008), and at 16 months after the treatment in one trial (Kenneth A Holroyd et al., 2010). They all showed reductions of the headache frequency.

Depressive symptoms were evaluated in five studies (35.71%) (Bromberg et al., 2012; Günther Fritsche et al., 2010; Hedborg & Muhr, 2011; Lemstra et al., 2002; Matchar et al., 2008) by different questionnaires: the Hospital Anxiety and Depression Questionnaire (Günther Fritsche et al., 2010), Depression Anxiety Stress Scale (Bromberg et al., 2012), the patient health questionnaire short-form (Matchar et al., 2008), the Montgomery–Åsberg Depression Rating Scale (Hedborg & Muhr, 2011), and the Beck Depression Inventory (Lemstra et al., 2002). All trials showed statistically significant post intervention outcomes, showing a reduction in depressive symptoms in two studies at 6 months (Bromberg et al., 2012; Matchar et al., 2008).

Quality of life could be measured with the SF-12 questionnaire that is divided into two parts: physical quality and mental quality, which were assessed in eight studies (57.14%). The physical quality of life showed statistically significant results in four trials (Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008; Seng & Holroyd, 2010) with the SF-36 questionnaire that was used in three of them (Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008) showing positive effects at 6 months, whereas the migraine specific quality of life questionnaire was used in one of them at 16 months (Kenneth A Holroyd et al., 2010).

The mental quality of life was measured with the SF-36 questionnaire in three studies and the Home Situation and Mood Questionnaire in one (Hedborg & Muhr, 2011) and showed increased scores in these four RCTs (Hedborg & Muhr, 2011; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008). One RCT showed significant out-comes at 6 months (Matchar et al., 2008) and another showed significant outcomes at 8 months in another (Hedborg & Muhr, 2011). The main results of each study are shown in **Table 2**.

– Meta-Analysis of Psychological Outcome Measures

Six RCTs evaluated the effects on depressive symptoms of TPE when compared with control groups. Meta-analysis of these studies showed no difference in the reduction of depressive symptoms in the short term (three studies (Bromberg et al., 2012; Günther Fritsche et al., 2010; Lemstra et al., 2002): N = 350, SMD = −1.48, 95% CI −3.34 to 0.36, *Z* = 1.57, *P* = 0.11; heterogeneity: *Q-value* = 107.2, *P* < 0.001; Figure 2). There was no evidence of publication bias (*P* = 0.36). There were also no changes in the intermediate term (four studies (Bromberg et al., 2012; Günther Fritsche et al., 2010; Hedborg & Muhr, 2011; Matchar et al., 2008): N = 692, SMD = −0.91, 95% CI −2 to 0.16, *Z* = 1.66, *P* = 0.09; *Q-value* = 93.3, P < 0.001; **Figure 2 A and B**). There was no evidence of publication bias (P = 0.33).

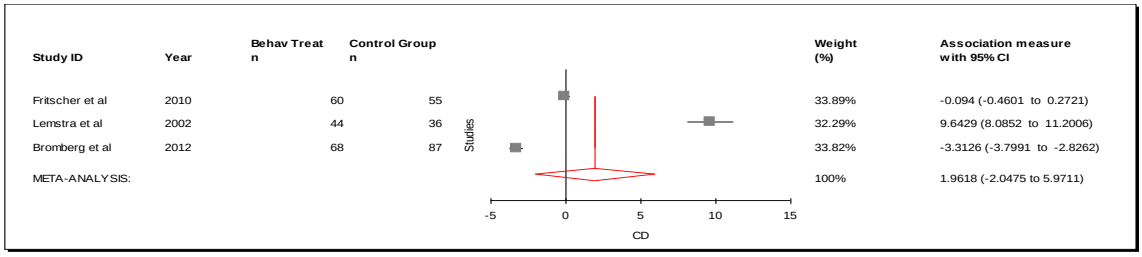


Figure 2A. Format plot of therpaeutic patient education (TPE) vs control group effect on depressive symptoms at short term

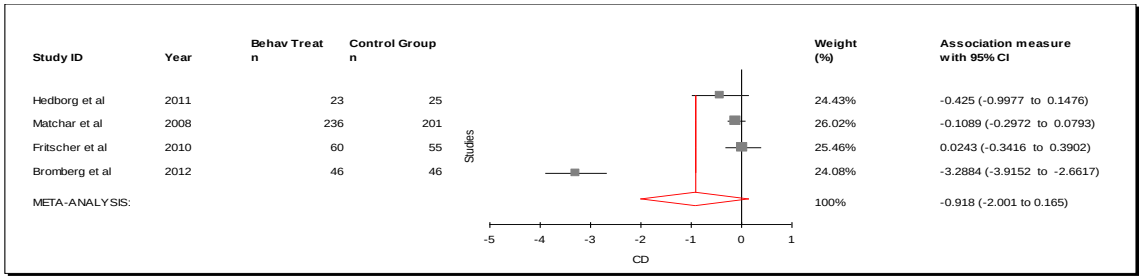


Figure 2B. Format plot of therpaeutic patient education (TPE) vs control group effect on depressive symptoms at intermediate term

TPE was significantly more effective when compared with the control group in improving the quality of life in the intermediate term (three studies (Kenneth A Holroyd et al., 2010; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008): N = 674, SMD = 0.36, 95% CI 0.05–0.67, Z = 2.28, P = 0.02; heterogeneity: Q-value = 6.26, P = 0.04; **Figure 3B**).

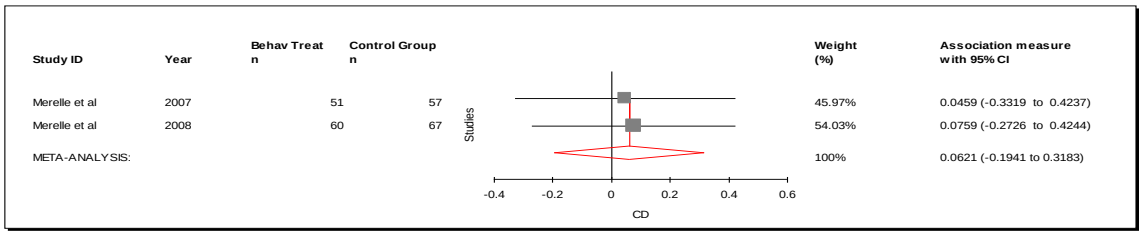


Figure 3A. Format plot of therpaeutic patient education (TPE) vs control group effect on quality of life at short term

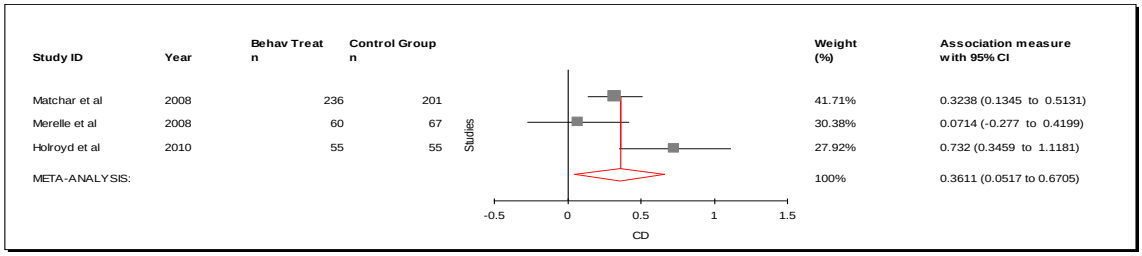


Figure 3B. Format plot of therpaeutic patient education (TPE) vs control group effect on quality of life at intermediate term

There were no differences in the short term (two studies (Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008): N = 245, SMD = 0.06, 95% CI −0.19 to 0.31, *Z* = 0.47, *P* = 0.63; heterogeneity: *Q-value* = 0.01, *P* = 0.9; **Figure 3 A**). There was no evidence of publication bias (*P* = 0.33).

Four RCTs that included self-efficacy variables were analyzed in the meta-analysis and showed no difference in the short term (three studies (Bromberg et al., 2012; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008): N = 390, SMD = 1.62, 95% CI −0.17 to 3.43, *Z* = 1.76, *P* = 0.07; heterogeneity: *Q-value* = 113.3, *P* < 0.001; Figure 4) or in the intermediate term (three studies (Lemstra et al., 2002; Saskia Y.M. Mérelle et al., 2008; Seng & Holroyd, 2010): N = 307, SMD = 2.44, 95% CI −0.03 to 4.92, *Z* = 1.93, *P* = 0.05, heterogeneity: *Q-value* = 135.8, *P* < 0.001; **Figure 4 A and B**). There was no evidence of publication bias for the meta-analysis in short-term outcomes (*P* = 0.14), but there was for the intermediate-term analysis (*P* = 0.03).

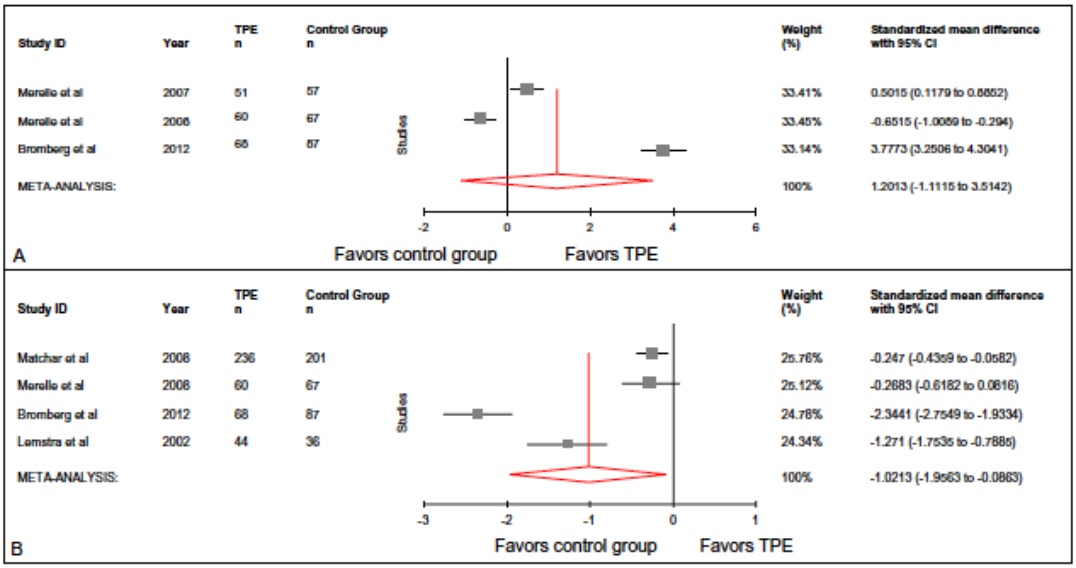


Figure 3B. Format plot of therpaeutic patient education (TPE) vs control group effect on self-efficacy at short (A) and intermediate (B) term

TPE was significantly more effective when compared with the control group at improving headache disability in the intermediate term (four studies (Bromberg et al., 2012; Lemstra et al., 2002; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008): N = 799, SMD = −1.02, 95% CI −1.95 to −0.08, Z = 2.14, P = 0.03; heterogeneity: Q-value = 93.1, P < 0.0001; Figure 5), but there were no differences in the short term (five studies (Bromberg et al., 2012; Günther Fritsche et al., 2010; Lemstra et al., 2002; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008): N= 585, SMD = −0.26, 95% CI −0.64 to 0.11, Z = 1.38, P = 0.16; heterogeneity: Q-value = 20.9, P = 0.0003; **Figure 5 A and B**). There was no evidence of publication bias for either of the two meta-analyses (short term, P = 0.88; intermedi-ate term, P = 0.27).

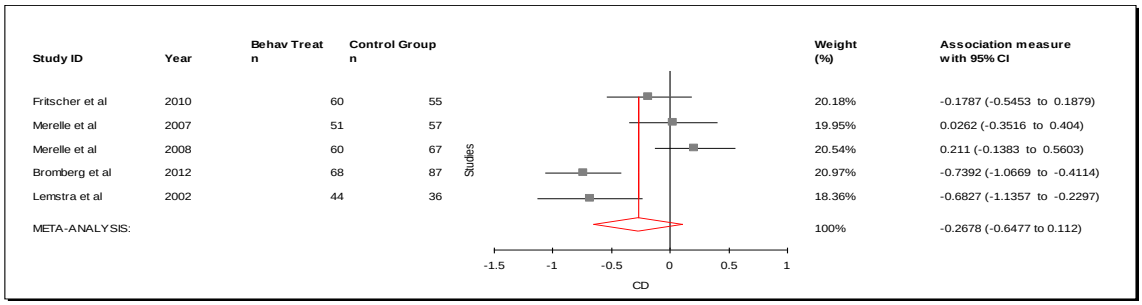


Figure 5A. Format plot of therpaeutic patient education (TPE) vs control group effect on disability at short term

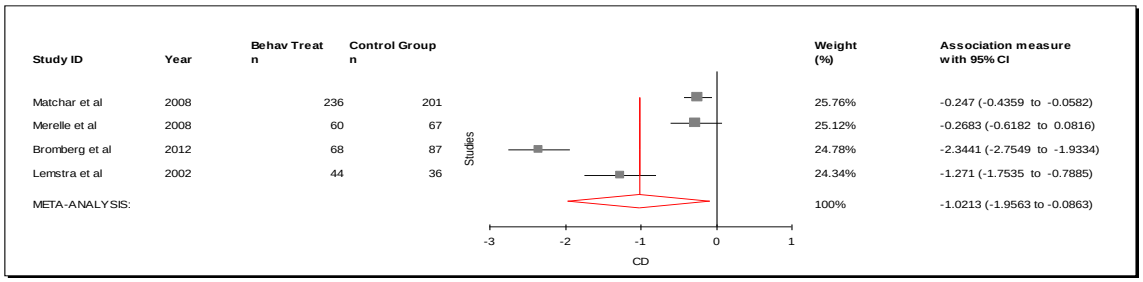


Figure 5B. Format plot of therpaeutic patient education (TPE) vs control group effect on disability at intermediate term

A total of seven RCTs evaluated the effects of TPE when compared with the control group on headache frequency. The meta-analysis for these studies showed difference in the reduction of headache frequency in the intermediate term (five studies (Bromberg et al., 2012; Günther Fritsche et al., 2010; Kenneth A Holroyd et al., 2010; Matchar et al., 2008; Saskia Y.M. Mérelle et al., 2008): N = 940, SMD = −0.24, 95% CI −0.48 to −0.01, *Z* = 2.05, *P* = 0.03; het-erogeneity: *Q-value* = 11.43, *P* < 0.02; **Figure 6 B**). There was no evidence of publication bias (*P* = 0.97). There were also no changes in the short term (four studies (Günther Fritsche et al., 2010; Lemstra et al., 2002; Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008): N = 430, SMD = −0.39, 95% CI −0.78 to 0.002, *Z* = 1.94, *P* = 0.05; heterogeneity: *Q-value* = 12.48, *P* = 0.005; **Figure 6 A**) and long term (two studies (Günther Fritsche et al., 2010; Kenneth A Holroyd et al., 2010): N = 115, SMD = 0.03, 95% CI −0.22 to 0.29, *Z* = 0.26, *P* = 0.78, heterogeneity; *Q-value* = 0.62, *P* = 0.43; F**igure 6 C**). There was evidence of publication bias for the meta-analysis in the short term (*P* = 0.02).

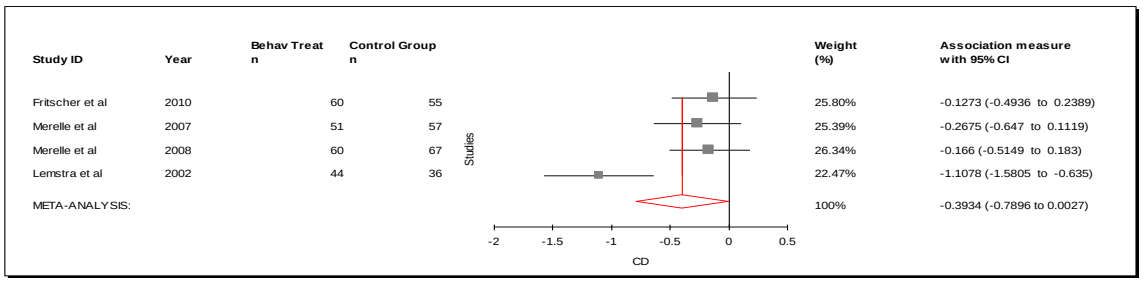


Figure 6A. Format plot of therpaeutic patient education (TPE) vs control group effect on headache frecuancy at short term

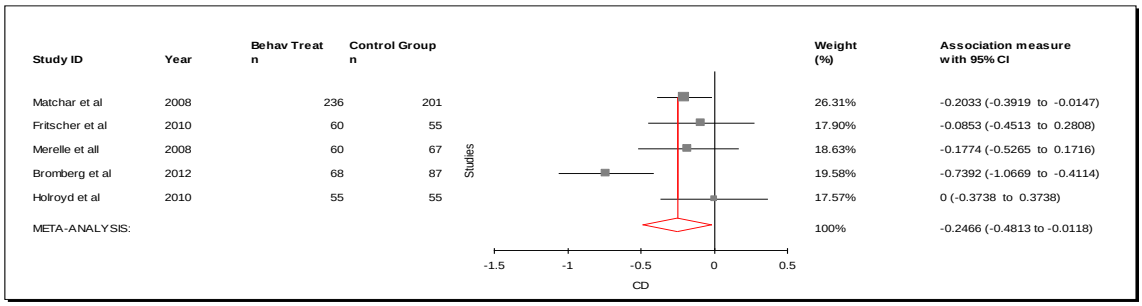


Figure 6B. Format plot of therpaeutic patient education (TPE) vs control group effect on headache frecuency at intermediate term

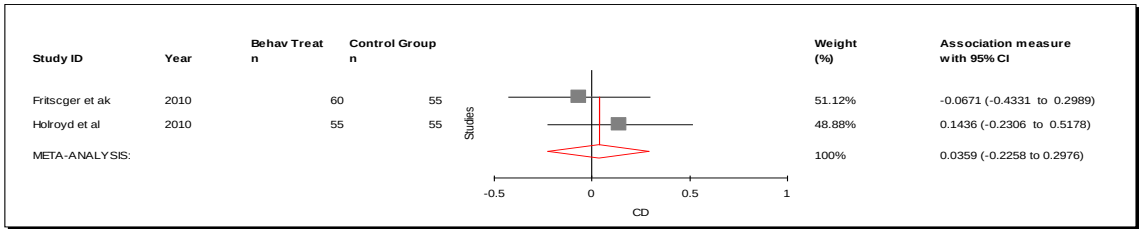


Figure 6C. Format plot of therpaeutic patient education (TPE) vs control group effect on headache frecuency at long term

4. DISCUSSION

This meta-analysis revealed that TPE provided improve-ments in disability and quality of life and decreased the frequency of migraines in the intermediate term. Finally, 14 studies were included, and the majority of them showed positive effects when treating migraine patients with TPE and other behavioral treatments. This intervention has been used to treat other chronic pain conditions, such as whiplash-associated disorders or lower back pain (Meeus, Nijs, Hamers, Ickmans, & Oosterwijck, n.d.-b; Nicholas & George, 2011). TPE is focused on improving coping strategies to reduce stress, increase relaxation, and internal locus of control (D'Souza, Lumley, Kraft, & Dooley, 2008).

Recently, another systematic review in German by Fritsche et al. summarized various forms of BBT for migraine (G Fritsche, Kröner-Herwig, Kropp, Niederberger, & Haag, 2013b). There were some differences with our review. For example, the inclusion and exclusion criteria, such as the kind of therapy included (biofeedback training and pro-gressive muscle relaxation), or population sample charac-teristics (children). In fact, these features differentiate our study from other systematic reviews or meta-analyses published. Most of these studies focus on children and adolescents, and study different

types of recurrent pain, including headaches (Eccleston et al., 2012; Hermann, Kim, & Blanchard, 1995; Pinquart & Shen, 2011; Trautmann, Lackschewitz, & Kröner-Herwig, 2006). Trautmann et al. recom-mended that future studies should identify the function of some mediators of self-efficacy and determine the effects of behavioral treatment on the quality of life (Trautmann et al., 2006).

Most of the published reports on migraines investigate the frequency of headaches, MIDAS, locus of control, self-efficacy, quality of life, and depressive symptoms. Five aspects regarding variables of the main analysis of the present study are discussed below.

In the present study, there were no indications that TPE reduced depressive symptoms. However, it is known that there are frequent symptoms in migraine patients in addi-tion to those experienced by those with chronic primary headaches (McMurtray, Saito, Diaz, Mehta, & Nakamoto, 2013). Unlike in our analysis, in another meta-analysis, TPE was effective for elevated depressive symp-toms in other chronic condition (e.g., for cancer patients) (Hart et al., 2012). It is possible that the presence or absence of pain may explain the difference between both studies. More-over, lacking knowledge of the baseline of pretreatment scores for the measures of depressive symptoms leave us thinking whether the problem was the lack of treatment effect or a floor effect where it is difficult to reduce the patient's symptoms significantly. Then, we must take into account that a possible floor effect could be in operation.

There are available several evidence based on psychologi-cal treatments to cope with depression, it probably referral high depressed migraine patients to them.

Finally, although there are numerous studies linking migraine with depression (Baskin & Smitherman, 2011; Bruti, Magnotti, & Iannetti, 2012; Lantéri-Minet, Radat, Chautard, & Lucas, 2005), and TPE seems to be an effective tool for decreasing the symptoms of depression (P R Martin, Nathan, Milech, & van Keppel, 1989), according to our results, TPE does not have much impact. This was unexpected as depression and anxiety are regarded as the most important psychosocial factors in episodic migraines becoming chronic (H. C. Diener, Küper, & Kurth, 2008), and we thought that TPE

would be effective. However, it is interesting to note that the isolated symptoms of depres-sion that are often comorbid with migraine are different from major depression, where symptoms occur with greater intensity.

It should be emphasized that in our meta-analysis, it was revealed that TPE improved the quality of life at the inter-mediate term. Additionally, all articles that analyzed this variable were of high methodological quality. This concept reflecting concern with the modification and enhancement of life attributes, for example, physical, political, moral and social environment; the overall condition of a human life (D'Amico, Grazzi, Usai, Leonardi, & Raggi, 2013). Similar to the conclusions that we reached, Nash et al. concluded that cognitive-behavioral treatment for chronic headache sufferers could improve quality of life (Nash, Park, Walker, Gordon, & Nicholson, 2004). It should be taken into account that one of the main predictors for the development chronic migraine is the damage to the quality of life (Siniatchkin, Riabus, & Hasenbring, 1999).

In social cognitive theory, self-efficacy has been consid-ered fundamental for obtaining a change in behavior (Bandura, 2004; Clark & Dodge, 1999) and has been regarded as an important factor mediating the outcome of headaches in behavioral studies (R. A. Nicholson, Houle, Rhudy, & Norton, 2007). Nevertheless, the effectiveness of TPE to increase self-efficacy in patients with migraine in the short term or intermediate term has not been observed. Other studies that have examined changes in headache self-efficacy using psychological treatment of migraine patients have suggested that headache self-efficacy increases substan-tially with cognitive behavioral therapy (R. Nicholson, Nash, & Andrasik, 2005b; Thorn et al., 2007). However, these studies had some limitations; studies without control groups cannot determine whether headache self-efficacy changes were due to intervention. The results of psychological variables in Mérelle's studies significantly changed during the short term and maintained the results up to 6 months in the internal locus of control, chance locus of control, and self-efficacy (Saskia Y.M. Mérelle et al., 2008; S Y M Mérelle et al., 2008). With good quality studies, Mérelle et al. in 2007 and Bromberg et al. in 2012 noted improvements in self-efficacy in migraine patients after receiving TPE (Matchar et al., 2008; S Y M Mérelle et al., 2008). We observed a non-significant trend in this outcome variable in the short term and intermediate term ($P = 0.07$ and $P = 0.05$, respec-tively). These results are also

supported by other studies, which show significant improvements in other variables, such as pain acceptance, pain catastrophizing, improved psychological distress, patient global impression of change, and positive pain coping strategies after behav-ioral interventions (Bromberg et al., 2012; Günther Fritsche et al., 2010). Some interesting correlations were obtained by Seng et al., who observed that patients with high baseline chance locus of control scores exhib-ited a larger increase in self-efficacy scores than partici-pants with low baseline chance scores, and subjects in the TPE group with low baseline internal locus of control exhibited larger increases in self-efficacy scale scores (Seng & Holroyd, 2010). However, the quality of this study was poor and had many limitations. We give some value to false beliefs and their relationship with self-efficacy improvements, considering that this fact seems to be important for the patient's recovery.

Intermediate-term improvements were found in headache disability when patients were treated with TPE. Disabilities associated with migraines are strictly related to its severity. Some areas remain functioning, such as communication, mobility, self-care, society activities, or relationships, whereas others are particularly affected (Leonardi, Raggi, Bussone, & D'Amico, 2010). An avoidance-based lifestyle may be extremely stressful, and this stress may produce chronic migraines and disability (Pistoia, Sacco, & Carolei, 2013).

In this work, three of the studies examined at intermediate term were high-quality studies and showed the most sig-nificant results of TPE in reducing disability in patients with migraines (Bromberg et al., 2012; Lemstra et al., 2002). Besides TPE, other interventions, such as physical therapy (Biondi, 2005; Campbell, Penzein, & Wall, 2000) or peripheral nerve stimulation, are also able to reduce disability in those complex treat-ment patients (Serra & Marchioretto, 2012; Silberstein et al., 2012). In this way, some authors suggest that earlier tertiary-level intervention may avoid the com-plications of migraine that occur in some patients and the increasing costs and utilization of care associated with higher disability (Freitag, Lyss, & Nissan, 2013).

Differences in the reduction of headache frequency in the intermediate term have been demonstrated. A good quality study by Bromberg et al. presented the most sig-nificant results at the intermediate term (Bromberg et al., 2012).

Headache frequency is the main issue for migraine patients and is strongly associated with increasing disabil-ity. Therefore, it is known that the combination of TPE and beta-blockers yield greater reduction in the frequency of headaches and days with headaches (Kenneth A Holroyd et al., 2010). It is possible that group interventions, as proposed by Lemstra et al., may be useful for patients as people tend to mirror them-selves on the others improving headache frequency, inten-sity and duration, quality of life, pain related disability, and depressive symptoms (Lemstra et al., 2002).

It is clear that improvements in disability, quality of life, and frequency of headaches were occurred in the intermediate term, but not in the short term. It might be too ambitious to aim for a significant decrease in these factors immedi-ately after the TPE due to the participants, as they may still be in the process of learning to adapt their lifestyle. According to the process of learning and memory, neces-sary time is required to consolidate the information received. The studies of Fuster and Alexander (published from 1971 and later) support the idea of memory consoli-dating in the intermediate/long term (Fuster & Alexander, 1971; Rains et al., 2005).

It is worth noting that this is the first meta-analysis that collected information about the clinical effectiveness of TPE for migraine and chronic migraine patients.

CHAPTER 4: Widespread mechanical hyperalgesia and its relationship with psychosocial variables in chronic migraine patients

1. INTRODUCTION

Zapaterra et al., (2011) showed that patients with chronic headaches presented allodynia and lower outcomes of cutaneous pressure pain thresholds (PPTs) compared with chronic individuals who presented episodic headache (Zappaterra et al., 2011). Moreover, patients with chronic and episodic migraines had lower PPTs in some cranial and cervical muscles compared with healthy subjects (Débora Bevilaqua Grossi et al., 2011).

The aim of this research was to determine differences in somatosensory and psychosocial outcomes between patients with chronic migraines and healthy subjects in both women and men, Palacios-Ceña et al., (Palacios-Ceña et al., 2016) studied pressure pain sensitivity in women with migraine, but did not study the association with psychosocial variables . In addition, our secondary aim was to evaluate the association between quality of life with PPTs and psychosocial variables in both groups. Gil-Martinez et al., (Alfonso Gil-Martínez et al., 2016) showed the relationship between somatosensory and psychosocial variables in chronic migraine but only in women as w they did not compare quality of life, depression and self-efficacy which have been demonstrated to be affected among patients with migraine when compared with healthy subjects.

2. METHODS

We conducted a cross-sectional study to assess differences in psychological and physical variables in patients with chronic migraines compared with healthy subjects. This study was performed in accordance with the STROBE statement (von Elm et al.). One assessor was previously trained with an expert in order to measure and assess the variables.

This study was approved by the ethics committee of CSEU (Centro superior de estudios Universitarios La Salle, Universidad Autónoma de Madrid , Spain record number CSEULS-PI-002-2013).

2.1. Participants

A total of 114 subjects were recruited for the study. We divided the subjects into two groups: the Chronic Migraine Group (CMG) and a healthy group (HG). The HG consisted of 62 volunteers (54 females and 8 males; mean age: 47.94±12.69 years; age range: 18–70 years). Every individual in this group was in a pain-free state. The CMG consisted of 42 females and 10 males (mean age: 49.02±13.90 years) recruited from a medical center (Unidad de Ciencias Neurológicas) between March 2013 and December 2015. The demographic characteristics of the subjects are listed in ***Table 1***. All of the subjects in this group were diagnosed with chronic migraines by a neurologist, following the ICHD-III (Road, 2013).

We selected the sample after assessing inclusion and exclusion criteria using non-probability sampling. Individuals who were interested in participating were assessed by a neurologist and a migraine diagnosis was conducted according to The International Classification of Headache Disorder criteria (Road, 2013). Patients included in CMG were selected as long as they fulfilled the following inclusion criteria: an age between 18 and 70 years, a diagnosis of chronic migraine with or without aura by the ICHD-III (Road, 2013).

The HG and CMG exclusion criteria were as follows: patients receiving physiotherapy treatment in the cervical or cephalic area, patients with severe cognitive deficits,

patients with degenerative neurological syndromes, patients with fibromyalgia and patients who had undergone a surgical procedure of the head, neck or shoulders.

The initial assessment aimed to check that the subjects met all of the inclusion criteria; we also excluded all of those patients who satisfied one or more of the exclusion criteria.

2.2. Instruments and measures

– *Quality of life*

We measured quality of life using a survey on the effect of headaches (HIT-6). This questionnaire measures how headaches affect patients with chronic pain in terms of activities such as work, social activities or home life via 6 items (Yang, Rendas-Baum, Varon, & Kosinski, 2011). The HIT-6 has been demonstrated to have acceptable psychometric properties (M. Martin, Blaisdell, Kwong, & Bjorner, 2004). **Appendix 1**

– *Catastrophizing*

To measure catastrophizing, we used the pain catastrophizing scale (PCS). It consists of 13 items that are associated with greater pain, increased behaviors toward pain, increased use of analgesics, decreased daily activities, incapacity and suicidal ideation (Olmedilla, Ortega, Boladeras, Abenza, & Esparza, 2008). This questionnaire has been validated in the Spanish language (Zafra, Toro, & Cano, 2013), and it exhibits good reliability and validity (García Campayo et al., 2008). **Appendix 2**

– *Depression*

We used the Beck Depression Inventory to measure depression. This inventory values the symptomatic intensity of depression on the basis of 21 items. There are four possible answers per item, which assess the severity and intensity of the symptom and are organized from least to most serious. The timeframe refers to the present and the previous week (Hayden, Brown, Brennan, & O'Brien, 2012; Kliem, Mößle, Zenger, & Brähler, 2014). The Spanish version of the Beck Depression Inventory has been shown to exhibit acceptable psychometric properties (Penley, Wiebe, & Nwosu, 2003). **Appendix 3**

– *Kinesiophobia*

To value the fear of movement, we used The Tampa Scale of Kinesiophobia (TSK-11). The shortened TSK-11 scale consisted of 11 items; each item has a score between 1 and 4. The TSK-11 is a brief, reliable and valid measurement of fear of movement or fear of reinjury for chronic pain patients (Tkachuk & Harris, 2012). It has been validated in the Spanish language in 2011, and it has been shown to have appropriate psychometric properties (Gómez-Pérez, López-Martínez, & Ruiz-Párraga, 2011). **Appendix 4**

– *Self-efficacy*

We used the Chronic Pain Self-Efficacy Scale to assess self-efficacy. This scale measures the ability of a subject with chronic pain to carry out activities in his or her daily life. The Chronic Pain Self-Efficacy Scale consists of 15 items that measure a subject's ability to do activities by him or herself and 6 items that measure the subject's ability to perform activities with help from another person (Martín-Aragón, M. Pastor, M. A. Rodríguez-Marín, J. March, M.J. Lledó, A. López-Roig, S. Terol, 1999). The Spanish version of the Chronic Pain Self-Efficacy Scale is a valid, reliable and useful tool for measuring self-efficacy (Martín-Aragón, M. Pastor, M. A. Rodríguez-Marín, J. March, M.J. Lledó, A. López-Roig, S. Terol, 1999). **Appendix 5**

– *Pressure pain thresholds*

The PPT is defined as the minimum amount of pressure needed to cause a sensation of pain (Roy La Touche et al., 2013). We measured PPTs using a digital algometer (FDX 25, Wagner Instruments, Greenwich, CT, USA). This measuring instrument is used for both therapeutic and diagnostic purposes. The reliability and validity of this instrument has been evaluated in several studies (Chesterton, Sim, Wright, & Foster, n.d.; Fern & Fern, 2004).

The algometer consists of a 1 cm^2 rubber disk attached to a pressure pole calibrated in kilograms. The measurements of thresholds are expressed in kg/cm^2, and the pressure ranges from 0–10 kg/cm^2 (F Antonaci, Sand, & Lucas, 1998). The protocol that we used included a sequence of 3 measurements with an interval of 60 seconds between each measurement. We then calculated the average of these three measurements.

The device was applied perpendicularly to the skin, and the patient was asked to inform the evaluator when the pressure started to change into a feeling of pain. At that point, the evaluator stopped applying pressure and recorded the value.

2.3. Procedure

The sample selection was made taking into account the inclusion and exclusion criteria of the study. Our sample patients were diagnosed with chronic migraines by a neurologist. All of the participants were presented with an information sheet about the study; the participants were asked to read this sheet and sign a form of informed consent.

Next, the subjects in both groups filled out the HIT-6, Self-efficacy scale, Beck, PCS and TSK-11 questionnaires. We then assessed PPTs using a digital algometer on the following points: Temporal 1, masseter 2, spinous process of C2, C5 zygapophyseal joints and the tibialis anterior.The points are located as shown in ***Figure 1***.

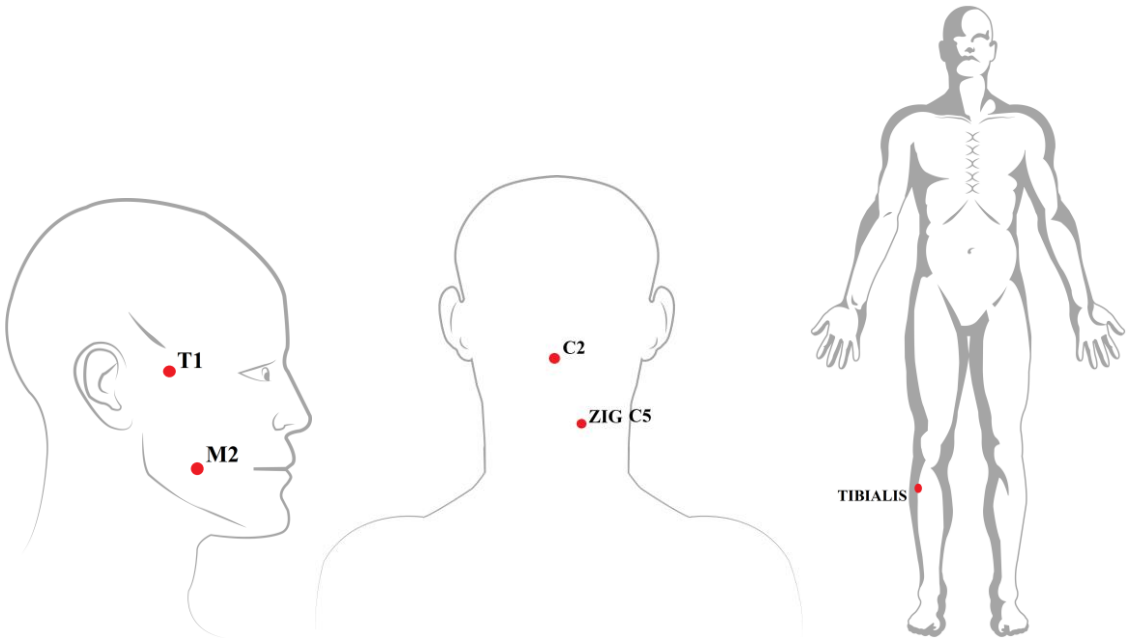


Figure 1. Points PPT
Abbreviations: M2= masseter 2; T1=temporary 1; Tibialis= tibialis anterioris; Zig C5= C5 zygapophysial joint; C2= Spinous process of C2

The patient was placed face up to assess the following areas:

- Masseter 2 bilateral: 1 cm superior and 2 cm anterior from the angle of the jaw

- Temporary 1 (anterior fibers of the muscle): 3 cm superior to the zygomatic arch in the middle point between the end of the eye and the anterior part of the helix of the ear.
- Tibialis anterior

Next, the patient was placed face down to assess the following areas:

- Spinous process of C2.
- C5 zygapophyseal joint bilateral: 2 cm lateral to the spinous process of C5.

The algometer's value was read in kg/cm^2.

These parameters were measured in patients with chronic migraines and healthy subjects in order to compare the results and corroborate our initial hypothesis.

– *Sample size*

The sample size was estimated using G*Power 3.1.7 software (University of Düsseldorf, Germany) (Faul, Erdfelder, Lang, & Buchner, 2007). The data processing was considered to be a power calculation to detect between-group differences in the primary outcome measures (PPT in M2). To obtain 90% statistical power (1-β error probability) with a α error probability of 0.05, a *t*-test based on the difference of two independent mean models and an effect-side of 0.67 was established using means and standard deviation of both groups. We estimated that at least 96 subjects would be required (i.e., 48 per group).

– *Analysis data*

We used the Statistical Package for Social Sciences (SPSS 21, SPSS Inc., Chicago, IL USA) software to perform the statistical analysis. We evaluated the normal distribution of the different variables using the Kolmogorov-Smirnov test. We also employed the chi-squared test to study the categorical variables. We used the unpaired Student's *t*-test to investigate differences between groups in terms of PPTs and psychosocial variables (i.e., quality of life, catastrophizing, kinesiophobia, depression and self-efficacy). To test the associations between psychosocial and somatosensory variables, we calculated Pearson's correlation coefficients. The classification of correlation coefficients was as follows: <0.30, low correlation; 0.30–0.60, moderate; >0.60 a significant correlation (Mukaka, 2012).

The analysis was conducted at the 95% confidence level, and a *P* value less than 0.05 was considered to be statistically significant.

3. RESULTS

From March 2014 until December 2015, 73 potentially eligible chronic migraine subjects were screened. Twenty-one of these subjects were excluded (28.73%) due to the following reasons: lots of data variables (n=18) and diseases that may interfere with the sensibility (e.g., as fibromyalgia (n=1) and viral diseases (n=1)), and an incorrect diagnosis of chronic migraine (n=1). Inclusion and exclusion of chronic migraine subjects and the final sample data are shown in the flow chart in ***Figure 2***. A total of 114 subjects were recruited for the study, and we divided these subjects into two groups: CMG and HG. The asymptomatic sample consisted of 62 volunteers (87.09% female) with an average age of 47.94±12.69 years. The CMG consisted of 52 volunteers (80.76% female) with an average age of 49.02±13.90 years. No differences were found between the groups in terms of the demographic characteristics listed in ***Table 1***.

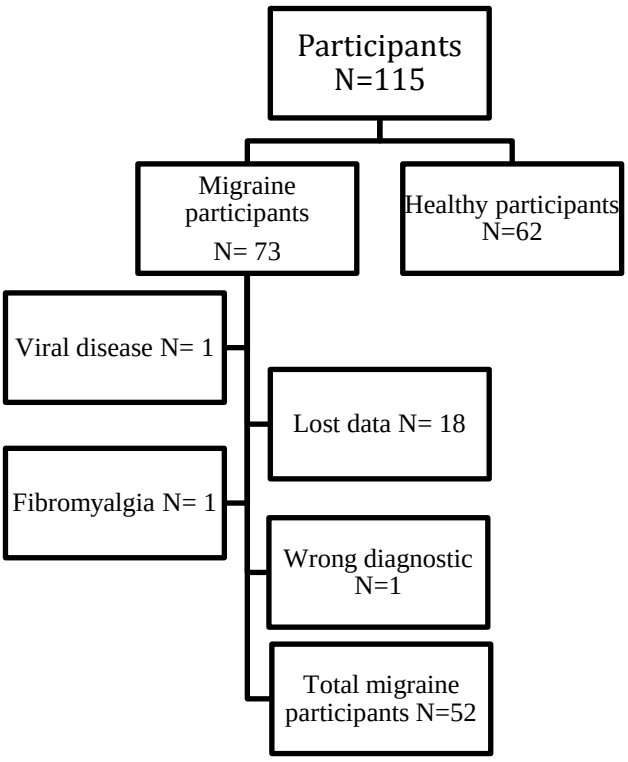


Fig 2. Flow Chart including and Withdrawal subjects

	Healthy Group N = 62	**Migraine N = 52**	
Age years	47.94±12.694	49.02 ±13.897	
Male/Female	8/54	10/42	0.442†
Height (cm)	164.68 ±7. 760	163.84 ± 8. 266	
Weight (Kg)	67.56 ±12. 330	65.49 ±17. 671	

Table 1. Demographic characteristics. Values are mean ± DS

† Chi-squere tests.

– *Pressure pain thresholds*

Our results revealed that patients with chronic migraines had lower PPTs in all of the following points compared with healthy subjects: Masseter 2 *P*<0.01 (1.300±0.665), Temporalis 1 *P*<0.01 (2.063±1.201), Tibialis *P*<0.01 (5.110±2.029), C5 zygapophyseal joint *P*<0.01 (2.330±1.280), spinous process of C2 *P*<0.01 (2.505±1.642). THese differences between groups are expressed as a mean±standard deviation with a 95% confidence level in ***Table 2***.

	Healthy Group N= 62	**Migraine N= 52**	***P***
M2	2,401 ± 0,767	1,300 ± 0,665	0.01**
T1	3.787 ± 1,263	2,063 ± 1,201	0.01**
TIB	7,546 ± 2,377	5,110 ± 2,029	0.01**
ZIG C5	3.771 ± 1,641	2,330 ± 1,280	0.01**
SPIN C2	4,562 ± 1,980	2,505 ± 1,642	0.01**

Table 2. Differences between physical variables. Values are mean ± DS ***P* <0.01
Abbreviations: M2= masseter 2; T1=temporary 1; Tib= tibialis anterioris; Zig C5= C5 zygapophysial joint; Spin C2= Spinous process of C2

– *Psychosocial variables*

The psychosocial variables listed in ***Table 3*** show that every variable except for kinesiophobia (*P*=0.680) exhibited a statistically significant difference between healthy subjects and chronic migraine patients.

	Healthy Group N= 62	**Migraine** N= 52	*P*
	Mean ± DS	Mean ± DS	
BECK	5.122 ± 4.790	11,265 ± 9.686	<0.01**
CADC	155,418 ± 23,503	123,625 ± 29,953	<0.01**
TSK -11	21,245 ± 6,247	20,694 ± 6,914	0.680
PCS	7,837 ± 7,554	21,740 ± 11,443	<0.01**
HIT-6		63,135 ± 8,044	<0.01**

Table 3. Differences between psychosocial variables. Values are mean ± DS ***P*<0.01
Abbreviations: BECK = beck depression inventory; CADC = Chronic Pain Self-efficacy Scale; TSK-11 = tampa scale of kinesiophobia; PCS = pain catastrophizing scale; HIT-6 = headache impact test-6;

– *Correlation analysis*

The association among psychosocial variables (quality of life, catastrophizing, kinesiophobia, depression and self-efficacy) and somatosensorial variables (M2, T1, Tib, Cig C5 and Spin C2) were examined using Pearson's correlation coefficients. ***Table 4*** lists the results of correlation analysis examining the bivariate relationships. The strongest association observed was found among the psychosocial variables themselves, even though correlations between psychosocial variables, was not the purpose of our study. The correlation was moderate between catastrophizing and PPTs in point 1 of the Temporalis muscle *(r*=-0.320; *P*<0.05) and catastrophizing and the C5 zygapophyseal joint PPT *(r*=-0.337; *P*<0.05). Quality of life was associated with PPTs in point 1 of the Temporalis muscle *(r*=-0.288; *P*<0.05), the tibialis muscle *(r*=-0.324;

P<0.05), the C5 zygapophyseal joint *(r*=-0.325; *P*<0.05) and the spinous process of the C2 point *(r*=-0.322; *P*<0.05).

	M2	T1	TIBIA	ZIG C5	SPINC2	BECK	CADC	TSK-11	PCS	HIT-6
M2		0.890**	0.773**	0.745**	0.782**	-0.26	0.010	-0.087	-0.202	-0.197
T1			0.849**	0.822**	0.802**	-0.110	0.150	-0.132	-0.320*	-0.288*
TIBIA				0.831**	0.807**	-0.217	0.223	-0.176	-0.267	-0.324*
ZIG C5					0.934**	-0.242	0.172	-0.269	-0.337*	-0.325*
SPINC2						-0.138	0.124	-0.229	-0.249	-0.322*
BECK							-0.612**	0.404**	0.531**	0.514**
CADC								-0.401**	-0.446**	-0.556**
TSK-11									0.351*	0.369**
PCS										0.636**
HIT-6										

Table 4. Pearson correlation for experimental group *P<0.05, **P <0.01. Abbreviations: M2= masseter 2; T1=temporary 1; Tib= tibialis anterioris; Zig C5= C5 zygapophysial joint; Spin C2= Spinous process of C2; BECK = beck depression inventory; CADC = Chronic Pain Self-efficacy Scale; TSK-11 = tampa scale

4. DISCUSSION

Our results revealed statistically significant differences between chronic migraine patients and healthy subjects in all somatosensory and psychosocial variables except for the kinesiophobia outcome. We also found associations between PPTs and psychosocial variables in chronic migraine patients, with no differences between genders.

A variety of theories have been developed about the origin and pathophysiology of migraines. We have found that all measured PPT points in the trigeminal and cervical areas were lower in migraine patients. This finding shows that chronic migraines may be explained by the physiopathology theory of central sensitization

This study found widespread mechanical hyperalgesia which could explain a central sensitization process. Central sensitization is explained by widespread mechanical hyperalgesia, widespread thermal hyperalgesia, and mechanical and thermal allodinia, as a consequence of an hiper-excitability of the central nervous system (Burstein, 2001).

Burstein R, et al. (Burstein, 2001) found that allodinia responses reflect a sensitization in trigeminal nucleus (facial allodinia) and thalamus (extracephalic allodinia). The

afferents of cervical (C5 zygapophysial joint and spinous process of C2) and trigeminal structures (point 1 of Temporalis muscle, and maseter 2 point muscle) are able to sensitize second-order neurons within the TCNC, leading either to a reduction of the thresholds or to an increased response of non-noxious stimuli (Andersen, Petersen, Svendsen, & Gazerani, 2015; Gonçalves et al., 2015). Skin and muscles of the face also send nociceptive afferents inputs to trigeminocervical neurons (Burstein, Yamamura, Malick, & Strassman, 1998). Magnetic resonance imaging data have shown that neurons from ventral posteromedial thalamic nuclei project afferences to somatosensory (primary and secondary) cortex and insula are related to the location, intensity of pain (Noseda et al., 2010; Noseda, Jakubowski, Kainz, Borsook, & Burstein, 2011). The results of our study reveal that PPTs in the tibialis anterior point are lower in chronic migraine patients compared with healthy subjects, which could showed that chronic migraine patients suffer from widespread mechanical hyperalgesia. Widespread mechanical hyperalgesia leads to the spreading of pain to non-injured areas; this process is caused by both peripheral and central mechanisms (Woolf, 2011). Central sensitization explains hyperalgesia (a painful stimulus perceived as being excessively painful), as well as the large reduction in pain thresholds and a greater extension of receptive areas in the dorsal horn of the spine (Meeus et al., 2008; Nijs et al., 2011).

Filatova et al., (Filatova, Latysheva, & Kurenkov, 2008) found that patients with chronic headache exhibit central sensitization (CS) during baseline suggesting that CS does not depend on clinical headache characteristics, but CS may be a mechanism of headache chronification and chronicity maintaining. Grossi et al., (Débora Bevilaqua Grossi et al., 2011) explain how a nociceptive sensitized path may increase muscle tenderness in migraine patients, indeed muscle tenderness could also contribute to CS. Our study provide original knowledge about male and female migraine patients with lower PPT in tibialis anterior point when compared with healthy subjects, it shows widespread mechanical hyperalgesia. Grossi et al., (Débora Bevilaqua Grossi et al., 2011) found that lowered PPT are migraine indicators, not being a frecuency indicator. Hypersensitivity or widespread of pain is probably caused by changes in central pathways of pain processing, particularly CS involving the TCNC (Finnerup et al., 2016; Schürks & Diener, 2008)

Migraine patients show cortical reorganization in anterior cingulate cortex area (Coppola & Schoenen, 2012), migraine medication over-users could facilitate central sensitization and increase headache frequency changing somatosensory evoked potentials. Cortical response about sensitivity in migraine patients, fluctuate over time, not only because of the relationship between migraine attacks periods but also because of the relationship in attacks frequency. (Coppola et al., 2010)

Quality of life, catastrophizing, depression and self-efficacy outcomes were statistically different between groups. Based on the literature, chronic pain patients exhibit increased psychosocial variables (G Fritsche, Kröner-Herwig, Kropp, Niederberger, & Haag, 2013a; Meeus, Nijs, Van Mol, Truijen, & De Meirleir, 2012; Ronald Melzack & Katz, 2013; R. A. Nicholson et al., 2007; Schmitt et al., 2009).

Pain involves a perceptual process in the brain that in turn involves suffering, pain behavior and variable disability that may affect mood (D C Turk, 1997). Whether pain becomes chronic is related to behavioral, psychological and neurobiological factors (Apkarian, 2008; Hashmi et al., 2013b). A recent study showed how the chronification of back pain changes brain representation from nociceptive circuits to emotional ones, turning the acute pain pattern into emotional distress (Hashmi et al., 2013b). It has been proved migraine as a cortical modification producer (Coppola & Schoenen, 2012) been also related with serotonin transmission changes , contributing to the development of depressive symptoms or even depression in chronic migraine patients (Bahra, Matharu, Buchel, Frackowiak, & Goadsby, 2001; Panconesi, 2008; Weiller et al., 1995).

The multidimensional experience of pain includes three dimensions: the sensory-discriminative, the motivational-affective and the cognitive-evaluative dimensions. The sensory-discriminative dimension may be directly related to anatomophysiological mechanisms, which is explained by the connections between nociceptive neurons from ventral posteromedial thalamic nuclei and the somatosensory cortex. The motivational-affective dimension, which is explained by the thalamic nuclei and the anterior cingulate cortex, involves a subjective experience of pain, particularly in aspects of suffering or emotional changes. The cognitive-evaluative dimension is directly related to the motivational-affective dimension and refers to beliefs, cultural values and

cognition such as self-efficacy, perceived control and the consequences of the pain experience (Sherman, Luo, & Dostrovsky, 1997).

We did not find that chronic migraine patients present kinesiophobia even though there are some other chronic pain diseases such as chronic low back pain (Altuğ et al., 2016) and chronic nonspecific neck pain (Lopez-de-Uralde-Villanueva, Beltran-Alacreu, Fernandez-Carnero, Kindelan-Calvo, & La Touche, 2016) that are associated with a fear of movement. There are controversial studies in the literature about range of motion in migraine patients, which may explain the absence of kinesiophobia in the present study. On the one hand, Jull et al., (Jull, Amiri, Bullock-Saxton, Darnell, & Lander, 2007) verified that the cervical range of motion in migraine patients was not decreased compared with patients suffering from cervicogenic headaches. However, Bevilaqua-Grossi et al., found that women suffering from episodic and chronic migraines have a reduced cervical range of motion compared with healthy subjects (Bevilaqua-Grossi et al., 2009; Carvalho et al., 2014).

In this study, we used self-reported questionnaires of psychosocial variables to identify possible associations with somatosensorial variables. Using linear regression analysis, we found that the impact of headache on quality of life and pain catastrophizing is associated with PPTs in both the trigeminocervical and extratrigeminal areas. We also found moderate associations between catastrophizing and PPTs in the temporalis point 1 muscle and the zigapophyseal process of C5, areas innervated by the trigeminal nerve and Cervical 4 and 5 root nerves, respectively. Goli Z et al., showed that catastrophizing is a misleading factor in the relationship between pain and mood in patients with migraines (Goli, Asghari, & Moradi, 2016). In another study, pain catastrophizing was shown to be a contributor to the chronification of mandibular muscle pain in patients with temporomandibular disorders (Velly et al., 2011).

Pain intensity, pain catastrophizing and quality of life were associated with chronic migraine patients in our study. Some other authors have also recovered these associations, which are independent of other psychosocial factors such as anxiety or depression (K A Holroyd, Drew, Cottrell, Romanek, & Heh, 2007).

A recent study demonstrated that pain catastrophizing moderated the pain intensity-interference relationship between headache pain intensity and pain interference in obese women with migraines. This finding was also strongly recovered in our study (Thomas et al., 2016).

In our results, quality of life was negatively correlated with pain severity in the trigeminal and extratrigeminal areas assessed using an algometer. However, quality of life was positively correlated with depression scores. In a recent study, identical results were found when studying children with migraines; quality of life and the degree of disability were also negatively correlated (Öztop et al., 2016).

We found that both men and women with chronic migraine had lower PPTs in the evaluated regions, as well as changes between psychosocial variables, when compared with the healthy subjects. Not finding any differences between genders is a controversial factor in patients with pain related to chronic diseases, according to the literature. A study supports our findings in children (Ferracini, Stuginsk-Barbosa, Dach, & Speciali, 2014). Even so, there is a large body of literature showing that women have a heightened perception of pain when pain is experimentally induced by jaw movement in masticatory muscles, when presenting temporomandibular disorders (Häggman-Henrikson, Osterlund, & Eriksson, 2004; Roy La Touche et al., 2015). According to migraine patients, previous studies have shown that women have greater mechanical hipersensitivity than men in their cervical muscles (Florencio et al., 2015) and that various biopsychosocial factors may contribute to pain perception (Racine et al., 2012). We believe that differences between gender may be more frequently found because migraines and other trigeminocervical-associated disorders are more prevalent in women (Hans-Christoph Diener et al., 2011) It is nowadays very important to measure gender differences in chronic pain patients, for example according to genetic relevance, mutations in the Mcl1 gene are associated with different κ-opioid analgesia responses in females (Mogil et al., 2003). There are also biological pathway differences, for example TLR4 pain is a pathway only found in males and is testosterone dependent (R. E. Sorge et al., 2011), Microglia activation in chronic pain has been found to only be relevant in male mice and is hormone dependent. Female mice depend on a t-cell mediated mechanism (Robert E Sorge et al., 2015).

CHAPTER 5: Temporal summation, widespread pain and its relationship with psychosocial variables in chronic migraine patients.

1. INTRODUCTION

The most recent lines of research have suggested that severe headache attacks involve the trigeminocervical complex (TCC) due to 2 underlying neuronal mechanisms: peripheral sensitization and central sensitization (Bartsch & Goadsby, 2003; Coppola et al., 2013; Goadsby, 2009).

Patients with CM experience pain in territories that belong to the division of the trigeminal and present various clinical conditions such as facial skin hypersensitivity, neck muscle sensitivity and hyperalgesia (Bigal & Lipton, 2008). This is theoretically due to the anatomical convergence of trigeminal afferent fibers and upper lumbar nerves, as well as to the sensitization of second-order neurons, which receive nociceptive trigeminal primary afferent neurons, during headache attacks (Aurora et al., 2011).

Other studies have shown that patients with CM have tenderness in the masticatory muscles (73%), neck tenderness (63%) and a greater prevalence of cervical pain than nausea (10,11). These findings suggest that there could be a pathophysiological relationship with other disorders, such as cranial-mandibular disorders, and therefore TCC sensitization (Marklund, Wiesinger, & Wänman, 2010a).

CM is also characterized by strong attacks of headaches, nausea, photophobia,

vomiting, sleep disorders and psychosocial disorders (de Tommaso et al., 2014). CM is considered one of the most significant causes of disability worldwide (Ghajarzadeh et al., 2014). Numerous studies have shown that individuals who experience CM have considerable social impairment (Ghajarzadeh et al., 2014; Stuginski-Barbosa et al., 2012).

Patients with CM can consume a high quantity of drug products, which can lead to secondary headaches due to medication abuse (Biagianti et al., 2014; Suh et al., 2012). Evers S et al. (Members of the task force: et al., 2006) showed that no drug is superior with regard to headaches. The lack of treatment homogeneity is explained by the controversy regarding the pathophysiology of migraines (Cioffi et al., 2014a).

The aim of this study is to demonstrate the influence of pain and psychosocial factors in patients with chronic migraine by comparing healthy patients and patients with migraines.

2. METHODS

– *Study design*

A descriptive, cross-sectional observational study was conducted at the La Salle Superior Center for University Studies (CSEULS) and the Neurological Sciences Unit (UCN) with patients recruited from October 2015 to May 2016. The study was authorized by the ethics committee of CSEULS (PI-035), and all procedures were approved according to the Declaration of Helsinki. The research study was conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

A single examiner conducted the data collection regarding the variables of interest. There was no masking in the measurements or in the patient follow-up.

- *Participants*

Fifty-two participants were recruited for the study and divided into 2 groups: a patient group with CM and a healthy participant group. The patients met the following criteria: between 18 and 75 years of age, CM diagnosed by a neurologist and able to read,

understand and be fluent in Spanish.

The exclusion criteria were fibromyalgia, an age below 18 years, undergoing physical therapy and illiteracy. For the healthy participant group, we excluded participants who had pain.

2.1. Variables and instruments

– *Pain intensity*

Pain intensity is the degree to which the participants perceive the manifestation of this phenomenon. The method used to assess the variable was the visual analog scale (VAS). This scale is validated for measuring pain intensity (Price, McGrath, Rafii, & Buckingham, 1983).

– *Quality of life*

Quality of life is the participants' subjective perception of their capacity to perform daily life activities. The scale employed was the Headache Impact Test (HIT-6) questionnaire, which assesses how headaches affect patients' quality of life. This questionnaire is validated in Spanish and has valid psychometric properties (M. Martin et al., 2004). **Appendix 1**

– *Pain expanse*

Pain expanse refers to the location of the pain in the body. A body chart was employed to evaluate pain location. The indicated areas were analyzed using 2 pieces of software: GIMP and ImageJ. Both programs have intraobserver and interobserver reliability (Dos Reis, de Barros E Silva, de Lucena, Mendes Cardoso, & Nogueira, 2016).

– *Depression*

According to the World Health Organization, depression is defined as a common mental disorder characterized by the presence of sadness, loss of interest or pleasure, feelings of guilt and various aspects that cause impairment in the patient. To assess these endpoints, we used the Beck Depression Inventory (BDI). The Spanish version shows acceptable psychometric properties (Penley et al., 2003). **Appendix 3**

– *Catastrophism*

Catastrophism is defined as a negative and increased mental perception regarding the phenomenon of pain, both actual and anticipated. The scale employed for the study was the Spanish version of the pain catastrophizing questionnaire (PCS). This questionnaire is validated in Spanish and shows good reliability and validity (García Campayo et al., 2008). **Appendix 2**

– *Kinesiophobia*

The fear of movement or kinesiophobia can be considered one of the predictors of the perpetuation and behavior of pain. The questionnaire employed for the study was the Spanish version of the Tampa Scale for Kinesiophobia (TSK). This questionnaire was validated in Spanish in 2011 (Gómez-Pérez et al., 2011). **Appendix 4**

– *Self-efficacy*

Self-efficacy for managing chronic pain is defined as the patient's capacity for controlling the pain (P. Kindelan-Calvo et al., 2014). The scale employed was the Self-Efficacy in Chronic Pain (SECP) questionnaire. This questionnaire is validated in Spanish (Martín-Aragón, M. Pastor, M. A. Rodríguez-Marín, J. March, M.J. Lledó, A. López-Roig, S. Terol, 1999). **Appendix 5**

– *Temporal summation*

Temporal summation or wind-up refers to the increase in perceived pain as the result of repeated harmful stimuli, performed at a frequency greater than 0.33 Hz. The repetitive stimuli were performed with 6.45 von Frey monofilaments (Cathcart, Winefield, Rolan, & Lushington, n.d.).

2.2. Procedure

The procedure began with the confirmation of the inclusion criteria in patients interested in participating. Once the patients were shown to have met the criteria, the procedure continued with reading and understanding the information sheet. Lastly, the participants signed the informed consent.

A single examiner was instructed by an expert physiotherapist for 60 minutes in the Neurological Sciences Unit to avoid potential biases.

After agreeing to participate in the study, the examiner delivered the patients the questionnaires to complete. The patients had to indicate the pain intensity at that moment, using the VAS.

The physical variables were then measured. Patients were given a drawing of the body on a DIN A4-size piece of paper and a red marker and instructed to indicate the areas where they felt pain. The body chart consisted of 5 figures (body 1, body 2, head 1, head 2 and head 3) (**Fig. 1***).*

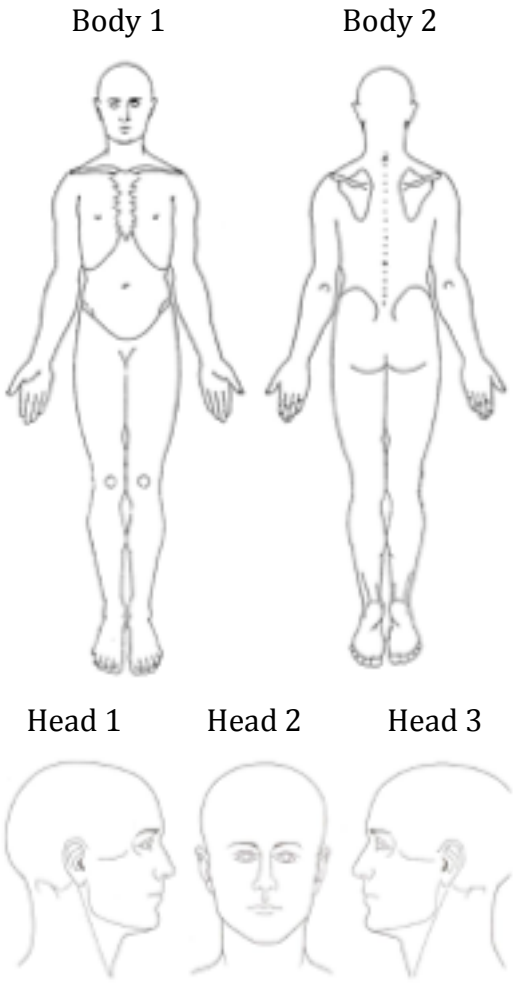


Figure 1. Body Chart

The assessment continued with the measurement of the temporal summation. First, the patient was placed in supine decubitus, and the following points on the dominant side were measured:

- Unilateral T1. The participant performed a contralateral rotation on the side being assessed. We located the midpoint of the eye line and the upper part of the ear on the side being assessed.

- Unilateral lateral epicondyle. We located the eminence through palpation.

Second, the patient was placed in prone decubitus with the hands resting on the forehead to measure the following points:

- Unilateral suboccipitals. The stimulus was administered to the external part of the lateral edge of the tendon of insertion of the upper trapezius fibers.

- Unilateral trapezius. The stimulus was administered 2.5 cm above the superior internal angle of the scapula.

For all points, a stimulus was administered, and the patient indicated (on the VAS) the degree of pain presented. Ten stimuli were then performed, with the patient indicating the pain on the VAS.

The procedure was performed equally for all patients in the group who showed no CM.

– *Sample size calculation*

The sample size was calculated using the G*Power 3.1.7 software (University of Düsseldorf, Germany) (Faul et al., 2007). For the calculations, we considered a base power for detecting differences between groups in the measures of the primary variable (temporal summation) in the epicondyle. To obtain a statistical power of 99% (1-β error probability) with a probability error (α) of 0.05, we employed a Student´s t-test model based on the difference between 2 independent means and an effect size of 1.28 using the previously established means and standard deviations for the 2 groups. We calculated that the study needed at least 40 patients (20 per group).

– *Statistical analysis*

This study employed the SPSS statistical package (SPSS 21, SPSS Inc, Chicago, IL USA). We used the Mann-Whitney U test to calculate the differences between the somatosensory and psychosocial variables between the healthy patients and the patients with chronic migraine. To calculate the relationship between the somatosensory and psychosocial variables, we calculated Spearman's correlation coefficient. All statistical analyses were performed based on a 95% confidence interval, and $p<0.05$ was considered statistically significant.

3. RESULTS

A total of 52 participants were included in the study from October 2015 to May 2016. The sample consisted of a healthy participant group (n=26) and a patient group with chronic migraine (n=26). The chronic migraine group was 88.46% women, and the experimental group had the same percentages. The demographic data are shown in **Table 1**.

	Migraine Group	**Healthy subjects**
	n=26	n=26
Age (years)	51,50(71,21)	53(71,20)
Females	23/26 (88,46%)	23/26 (88,46%)
Males	3/26 (11,54%)	3/26 (11,54%)
weight	63(96,49)	60(82,50)
Height	161,50(178,145)	167,50(181,156)

Table 1. Demographic Characteristics. Values are median (interquertile range)

We performed the Shapiro-Wilk statistical test, which showed that only height ($p=0.827$), kinesiophobia ($p=0.112$) and head 3 on the body chart ($p=0.069$) had a normal distribution ($p>0.05$). We therefore employed the nonparametric Mann-Whitney U test, because most of the variable did not show normality.

– *Physical variables*

In the descriptive data analysis, the Mann-Whitney U test revealed that for the physical variables temporal summation (T 1 p=0.001), (T 10 p=0.000), (EPIC 1 p=0.000), (EPIC 10 p=0.000), (OCCIP 1 p=0.000), (OCCIP 10 p=0.000), (TRAP 1 p=0.001), (TRAP 10 p=0.000) and visual analog scale (VAS=0,000) there was a statistically significant difference for all the stimulated points, given that p<0.01. The results of the physical variables are shown in **Table 2.**

	Migraine Group N=26	**Healthy Subjects N=26**	**p**
TS T1 1	1(6,0)	0(3,0)	0,001**
TS T1 10	3,50(8,0)	0(4,0)	<0,001**
TS EPIC 1	2(6,0)	0(2,0)	<0,001**
TS EPIC 10	4(8,0)	0(4,0)	<0,001**
TS OCCIP 1	2(8,0)	0(1,0)	<0,001**
TS OCCIP 10	5(9,0)	0(3,0)	<0,001**
TS TRAP 1	1,50(8,0)	0(1,0)	0,001**
TS TRAP 10	3,50(8,0)	0(3,0)	<0,001**
VAS	40,50(81,0)	0(50,0)	<0,001**

Table 2. Differences between physical variables. Values are median*(interquertile range)p<0,01** ST= temporal sumation; T1= temporary 1 estimulus; T10= temporary 10 estimulus; Epic 1= epycondile 1 estimulus; Epic 10= epycondile 10 estimulus; Occip 1= occipital 1 estimulus; Occip 10= occipital 10 estimulus; Trap 1= trapezius 1 estimulus; Trap 10= trapezius 10 estimulus VAS=Visual Analogic Scale*

– *Psychosocial variables*

In terms of the psychosocial variables, we found that there were statistically significant differences in all variables, except for TSK (p=0.273). The results of the psychosocial variables are shown in **Table 3.**

	Migraine Group N=26	Healthy Subjects N=26	p
CADC	123(169,60)	164,50(190,94)	<0,001**
PCS	20(44,5)	6(26,0)	<0,001**
TSK	22(33,11)	20(36,12)	0,273
BECK	7,50(43,0)	4(12,0)	0,003**
HIT-6	64(78,50)	42(65,36)	<0,001**

Table 3. Differences between psychosocial variables. Values are median (interquertile range)
*p<0,01***
CADC= Chronic Pain Self-efficacy Scale; PCS= pain catastrophizing scale; TSK-11= Tampa scale; BECK= Beck de depresion inventory; HIT-6= Quality of life scale

– *Correlation analysis*

Finally, we performed a correlation analysis between the physical and psychosocial variables, using Spearman's Rho test for nonparametric correlations. The interpretation was based on the following classification (Mukaka, 2012): very high correlation (0.9-1), high correlation (0.70-0.90), moderate correlation (0.50-0.70), low correlation (0.30-0.50) and negligible correlation (0-0.30).

With regard to the physical variables, there was a low correlation between the body 1 drawing on the body chart and the temporal summation in the temporal 1 stimulus (Rho=0.425), as well as between the VAS and the temporal summation in the trapezius 1 stimulus (Rho=0.458). In terms of the psychosocial variables, there was a low correlation between HIT-6 and SECP (Rho=-0.481) and PCS (Rho=0.472), as well as a moderate correlation with the BDI (Rho=0.548). Therefore, when a headache occurs and represents an impact on the patient's quality of life, there is an increase in catastrophism and depression and a reduction in self-efficacy. There was also a moderate correlation between the BDI and PCS (Rho=0.566), in other words, the more depressive traits a patient displays, the greater their levels of catastrophism. Lastly, in terms of the comparisons between physical and psychosocial variables, we found a low correlation between the body 2 drawing of the body chart and TSK (Rho=0.475). There was also a low correlation between VAS and BDI (Rho=0.436). The results are shown in **Table 4**.

	CADC	PCS	TSK	BECK	HIT6
T1	0,03	0,236	0,151	-0,081	-0,107
T10	-0,217	0,363	0,082	-0,014	-0,14
EPIC1	-0,001	0,299	0,188	-0,156	-0,235
EPIC10	-0,095	0,255	0,116	-0,142	-0,264
OCCIP 1	0,065	0,097	0,025	-0,151	-0,164
OCCIP 10	-0,102	0,275	-0,021	-0,156	-0,164
TRAP 1	0,101	0,114	0,004	0,013	-0,266
TRAP 10	-0,022	0,22	0,135	-0,037	-0,158
body 1	-0,269	0,175	0,102	0,073	0,395
body 2	0,028	-0,201	0,475*	0,082	0,106
head 1	-0,198	-0,138	0,003	-0,124	0,058
head 2	-0,022	0,128	0,124	-0,075	0,318
head 3	-0,114	0,14	0,076	-0,064	-0,034
Total	-0,024	0,061	0,21	-0,057	0,224
VAS	-0,284	0,321	0,298	0,436*	0,276

	CADC	PCS	TSK	BECK	HIT-6
CADC	1				
PCS	-0,518*	1			
TSK	0,392	0,282	1		
BECK	-0,508*	0,566**	0,35	1	
HIT-6	-0,481*	0,472*	0,344	0,548**	1

Table 4. Spearman Correlation in Migraine Group

CADC= Chronic Pain Self-efficacy Scale; PCS= pain catastrophizing scale; TSK-11= Tampa scale; BECK= Beck de depresión inventory; HIT-6= Quality of life scale;
ST= temporal sumation; T1= temporary 1 estimulus; T10= temporary 10 estimulus; Epic 1= epycondile 1 estimulus; Epic 10= epycondile 10 estimulus;
Occip 1= occipital 1 estimulus; Occip 10= occipital 10 estimulus; Trap 1= trapezius 1 estimulus; Trap 10= trapezius 10 estimulus VAS=Visual Analogic Scale

4. DISCUSSION

This study shows that patients with CM have an abnormal temporal summation when compared with the control group. Staud et al. (Staud, Weyl, Riley, & Fillingim, 2014) found that temporal summation is a useful tool for assessing and treating central sensitization in chronic processes. Therefore, CM shares clinical conditions with other chronic disorders such as chronic lumbar pain (CLP), fibromyalgia and temporomandibular joint disorders, given that the wind-up phenomenon also occurs in these conditions (Freitag et al., 2013; Latremoliere & Woolf, 2009; Staud et al., 2014).

Stuginski-Barbosa J et al. (Stuginski-Barbosa et al., 2010) observed that patients with CM were more susceptible to showing pain in the mastication-related muscles. This finding revealed a possible relationship between the pathophysiology of temporomandibular disorders and CM (Bartsch & Goadsby, 2003).

Our results show statistically significant differences in the temporal summation in the epicondyle between patients with CM and healthy participants. This finding suggests that patients with CM show mechanical hyperalgesia in an area noninnervated by trigeminal structures. Staud et al. showed that patients with fibromyalgia showed hyperalgesia in various areas, which relates this phenomenon with central sensitization (Staud, Robinson, & Price, 2007).

This study shows that the patients with CM had greater pain intensity under normal conditions than the asymptomatic participants. Latremoliere et al. (Latremoliere & Woolf, 2009) stated that a painful stimulus maintained over time produces hyperexcitability of the medullary and supramedullary neurons. Other authors have stated that central sensitization is also characterized by an impairment of descending inhibitory mechanisms responsible for pain modulation (Meeus et al., 2008).

Differing results were found in the psychosocial variables between the 2 groups. The literature has abundant information on the psychosocial changes presented by patients with chronic pain (Hashmi et al., 2013b; Kröner-Herwig & Gassmann, 2012). Baliki et al. (Amelia A Mutso et al., 2014) suggested that there is an impairment of the emotional circuits in the brains of patients with CLP.

Therefore, the pain is studied from the perspective of the biopsychosocial paradigm and is understood as a multidimensional experience composed of 3 dimensions: sensory-discriminative, cognitive-evaluative and affective-emotional (Melzack, 2001).

The literature suggests that patients with CM also show psychosocial changes that reduce the quality of life and increase anxiety, depression and social, affective and professional limitations (Fabio Antonaci et al., 2011). Guitera et al. (Guitera, Muñoz, Castillo, & Pascual, 2002)demonstrated that patients with CM showed a reduction in all aspects related to quality of life. Harris et al. (Harris, Loveman, Clegg, Easton, & Berry, 2015) emphasized the importance of psychosocial factors, specifically depression, which can be up to 3-fold greater in patients with CM than in asymptomatic individuals.

In the present study, we found no differences between the 2 groups in terms of kinesiophobia, despite the fact that other chronic processes present fear of movement (Lopez-de-Uralde-Villanueva et al., 2016). Antunes et al. (Antunes et al., 2013) showed that patients with CLP had greater fear of movement, of physical activity and of exercise when compared with healthy individuals. This finding could be due to the fact that the pain caused by CM is not due to the performance of movements, unlike CLP (Antunes et al., 2013).

In this study, we found no high correlations between the physical and psychosocial variables. We found a low correlation between depression and pain intensity, a finding that could be related to the perpetuation of pain over time. However, central sensitization can be understood as a process in which psychosocial and somatosensory factors are related in a neurobiological context (Curatolo et al., 2006).

CHAPTER 6. Biobehavioral Physical Therapy Strategies Based on Therapeutic Exercise Applied to Chronic Migraine Patients

1. INTRODUCTION

A growing body of research is showing the benefits of behavioral therapy for pain management, approaches based on the behavioral therapy as therapeutic patient education, therapeutic exercise have been demonstrated to be effective in some chronic diseases (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, et al., 2015).

Manual therapy has been applied Chronic pain patients and also in migraine patients (Cleland & Palmer, 2004; Hoving et al., 2006). Therapeutic patient education and therapeutic exercise are techniques demonstrated effectives in migraine patients (Gil-Martínez et al., 2013; Kindelan-Calvo et al., 2014).

We believe that the combination of behavioral approaches plus manual therapy could be better to improve quality of life in Chronic migraine patients than those separately.

The purpose of this study is to analize which combination of biobehavioral treatments are the most effective in patients with chronic migraine. The study design is a simple blind randomized controlled trial (outcomes assessor).

2. METHODS

2.1. Participants

A total of 65 men and women aged between 18 to 80 years old with chronic migraine

were included for the study. The patients were diagnosed by a neurologist with broad experience in headaches in Unidad de ciencias neurológicas (Madrid) and Hospital de la defensa Gómez Ulla (Madrid) following the ICHD-III (Road, 2013).

Patients included in the study were selected as long as they fulfilled the following inclusion criteria: Men and women aged from 18 to 80 years old with chronic migraine for at least 12 weeks; a diagnosis of chronic migraine with or without aura by the ICHD-III (Road, 2013); neck, shoulder or spine pain for at least 12 weeks; and a willingness to undergo the treatment.

The exclusion criteria were as follows: patients receiving physiotherapy treatment in the cervical or cephalic area; patients with severe cognitive deficits; patients with degenerative neurological syndromes; patients with fibromyalgia; and patients who had undergone a surgical procedure of the head, neck or shoulders.

2.2. Design

The study was a single-blinded randomized controlled trial. People with chronic migraine were recruited by referral from Unidad de ciencias Neurológicas clinic in Madrid. The trial was conducted in accordance with the CONSORT statement and approved by the ethical committee of Centro superior de estudios universitarios La Salle Approval Number: CESEULS-PI-002/2010 and was registered with the United States Clinical Trials Registry (registration number NCT02514148).

2.3. Instruments and variables

- Primary outcomes

Pain intensity

Pain intensity is the degree to which the participants perceive the manifestation of this phenomenon. The method used to assess the variable was the visual analog scale (VAS). This scale is validated for measuring pain intensity (Zafra et al., 2013).

Quality of life

Quality of life is the participants' subjective perception of their capacity to perform daily life activities (García Campayo et al., 2008). The scale employed was the Headache Impact Test (HIT-6) questionnaire, which assesses how headaches affect patients' quality of life. This questionnaire is validated in Spanish and has valid psychometric properties (Hayden et al., 2012). **Appendix 1**

- Secondary outcomes

Self-efficacy

Self-efficacy for managing chronic pain is defined as the patient's capacity for controlling the pain. The scale employed was the Self-Efficacy in Chronic Pain (CADC) questionnaire. This questionnaire is validated in Spanish (Martín-Aragón, M. Pastor, M. A. Rodríguez-Marín, J. March, M.J. Lledó, A. López-Roig, S. Terol, 1999). **Appendix 5**

Depression

According to the World Health Organization, depression is defined as a common mental disorder characterized by the presence of sadness, loss of interest or pleasure, feelings of guilt and various aspects that cause impairment in the patient. To assess these endpoints, we used the Beck Depression Inventory (BECK). The Spanish version shows acceptable psychometric properties (Penley et al., 2003). **Appendix 3**

Drug consumption

Latineen index is a questionnaire with 5 items, it assess pain intensity, pain frecuency, drug consumption, disability and sleep hours. It has been validated to use it in Spanish (Monsalve V, Soriano J, 2006). **Appendix 6**

Neck disability

Neck disability index is validated in Spanish questionnaire with 10 sections. It is a Likert scale with 6 options in each section, it means different levels of neck function. It has a good test retest reliability (0.978) and it is valid to Rank neck disability (Andrade

Ortega, Delgado Martínez, & Ruiz, 2010) **Appendix 7**

Catastrophizing

Catastrophism is defined as a negative and increased mental perception regarding the phenomenon of pain, both actual and anticipated. The scale employed for the study was the Spanish version of the pain catastrophizing questionnaire (PCS). This questionnaire is validated in Spanish and shows good reliability and validity (García Campayo et al., 2008) **Appendix 2**

2.4. Procedure

After reading and signed the informed consent and asking any questions they had, each patient was randomly allocated to one of the four groups by a therapist according to a random allocation list generated by a computed program (Graph Pad software, Inc CA 92037 USA). The randomized controlled trial was made up for physical therapists, two assessors and one therapist. One of the assessors made the appointments, discussed inclusion and exclusion criteria and generate the random numbers. The other assessor collected the baseline data and explain the functioning of the web page, helped them to make the registration and explained how to fill the questionnaires. In baseline and follow up periods, the outcome data recruitment was blinded because the web page (www.paulakindelan.net) designed for the study make it with any human help.

- Interventions

Patients were treated by combination of techniques regardless of their allocation group. In a month and a half period, all participants received six treatment sessions (once per week). Each session was one on one, and there was a rest period of a week between them. To enter the analysis, each patient have to attended at least 5 sessions.

The patients were randomized subdivided in four groups - one control and three experimental groups; the therapeutic education plus therapeutic exercise group (group 0), therapeutic education plus manual therapy plus therapeutic exercise group (group 1), therapeutic education group (group 2) and control group (group 3). We explain below, each one of them.

No Intervention Control group

No therapeutic intervention are being giving to this group of patients, they only will have their neurologist previously prescribed pharmacological treatment. This control group is measured on the whole range of variables in chronic migraine patients to compare it with experimental interventions

Experimental: Therapeutic exercise (TE)

The intervention giving to the patients consist on a therapeutic exercise protocol based on neck and low intensity general exercises. Therapeutic exercise consist on stretching the cervical-scapular muscles (Trapezius and angular of the scapula), Cranium-cervical flexor stabilization exercise, auto cervical tractions, shoulders rotation, low intensity exercise (walking), craniocervical extension, cervical flexion and extension.

Experimental: Therapeutic patient education (TPE)

The intervention giving to the patients consist on a therapeutic patient education based on pain neurophysiology protocol. Therapeutic patient education based on pain physiology from a biobehavioral perspective adding a training in coping strategies.

Experimental: Manual therapy (MT)

The intervention giving to the patients consist on a manual therapy techniques protocol. Manual therapy consist on; oscillatory traction; maintained craniocervical traction, upper cervical flexion mobilization, side glide roll, anterior-posterior upper cervical mobilization with wedge, lateral glide at the C1-C2 and C2-C3 levels, retraction technique, trigeminocervical neural mobilization , and upper cervical traction, followed by posterior-anterior glide at C4.

- Data Analysis

The HIT-6 was chosen as the primary outcome measure. The effect size of the HIT-6 was estimated to be medium (effect size, 0.2). With a power of 0.95 and an α level of 0.05, it was estimated that 16 participants would be required for each group (64 chronic migraine altogether) by using the software G*power 3.1 (Faul, Erdfelder, Buchner, & Lang, 2009). The enrolment goal was set at 77 participants to account for a 20% possible dropout rate. Baseline demographic characteristics are reported in ***Table 1.***

The Statistical Package for the Social Sciences (SPSS 21, SPSS Inc, Chicago, IL) was used for statistical analysis. The normal distribution of all primary and secondary measures data was assessed using the Shapiro-Wilk test (P > 0.05). The data showed a normal distribution. An independent t test and one-way analysis of variance (ANOVA) were used to compare variables from the three groups to baseline data.

For outcome variables, a two-way repeated measures within-between interaction factors ANOVA was performed; the factors analyzed were group (0 TPE+TE, 1 TPE+TE+TMO, 2 TPE, 3 Control group) and time (pre 0 weeks, post 6 weeks). Effect sizes (Cohen´s d) were calculated for the primary and secondary outcome variables. The magnitude of the effect was classified as small (0.20 to 0.49), medium (0.50 to 0.79), or large (0.8) according to Cohens method (Parker & Hagan-Burke, 2007). Comparison changes in primary and secondary variables over time of each treatment group are shown in ***Table 2.***

3. RESULTS

Sixty-five patients (10 males and 55 females) with chronic migraine were included. Patients aged between 18 to 74 (50.85 ±13.98) and a body-mass index BMI (24.74 ±5.37) participated in the study and were assigned to one of the four groups. No significant differences were found between groups for age (F= 1.127, P=0.346) gender (F= 0.994 , P=0.42), BMI (F= 0.495 , P=0.687), pain intensity (F= 0.476, P=0.700), self-efficacy (F= 0.259 , P=0.855), quality of life (F= 0.47, P=0.986), catastrophizing (F= 0.464 , P=0.708), drug consumption (F= 0.240, P=0.868), depression (F= 1.764, P=0.168), or neck disability (F= 0.602, P=0.617).

Demographic and clinical data for each group are detailed in ***Table 1***. There weren´t any secondary or adverse effect registered after any of the three groups treatment application.

	Group 0	group 1	group 2	Group 3	F (anova un factor)	P value
	N=20	N=15	N=17	N=13		
gender female (%)	18 (90%)	13 (86.6%)	16 (94%)	9 (69,23)	0.994	0.42
age (years)	47.24±13.48 (22 to 69)	55.93±10.84 (32 to 72)	49.35±13.19 (24 to 71)	51.69±18.09 (18 to 74)	1.127	0.346
BMI (body-mass index)	23.82±4,74 (18.75 to 38.81)	26.16±5.12 (20.13 to 34.62)	24.57±4.38 (19.94 to 34.25)	24.68±7.50 (16.22 to 45.72)	0.495	0.687
VAS	37.10±31.75(0 to 98)	38.13±26.69 (0 to 73)	41.80±28.03 (0 to 90)	28.42±30.83 (0 to 81)	0.476	0.700
CADC	85.55±52,73 (0 to 162)	74.20±45.74 (0 to 154)	86.18±47.30 (0 to 152)	91.08±68.53 (0 to 162)	0.259	0.855
HIT-6	63.95±10.44 (45 to 78)	63.80±6.39 (51 to 64)	64.27±6.91 (54 to 68)	64.85±6.20 (51 to 78)	0.47	0.986
PCS	22.85±13.73 (5 to 43)	25.27±9.72 (8 to 44)	20.67±9.46 (5 to 35)	21.38±11.53 (9 to 44)	0.464	0.708
DRUGS Latineen	1.40±1.18 (0 to 4)	1.53±1.06 (0 to 3)	1.73±1.38 (0 to 4)	1.64±1.12 (0 to 3)	0.240	0.868
BECK	13.38±9.89 (0 to 37)	7.92±6.35 (1 to 26)	15.21±10.24 (3 to 36)	17.33±14.76 (2 to 43)	1.764	0.168
IDC	20.13±12.10 (0 to 46)	26.83±15.36 (8 to 58)	25.54±15.70 (8 to 62)	26.18±16.43 (0 to 48)	0.602	0.617

Table 1: Demographic and clinical data of three groups at the beginning of the study.* P< 0.05 *** P< 0.01 VAS (Pain intensity); CADC (self-efficacy); HIT-6 (quality of life); PCS (Catastrophizing); Drugs Latineen (Drug consumption); BECK (Depression); IDC (cervocal disability); group 0 (TPE+TE); group 1 (TPE+TE+TMO); group 2 (TPE); group 3 (Control group)

– VAS (Pain Intensity)

All groups presented statistically significant differences between baseline outcomes and post-treatment ones ($P< 0.05$) in the intensity of pain variable, except for control group (F= 5.50, $P> 0.05$). The effect size (Cohen´s d) for baseline outcomes at post-treatment follow-up was greater for TPE group (d= 0.75) being small for control group and TPE plus TE group (d= 0.49 and d=0.34) for group TPE effect size was medium (d=0.62). Comparisons between groups of the baseline and post-treatment follow-up are presented in ***Table 2.***

– HIT-6 (Quality of life)

All groups presented statistically significant differences between baseline outcomes and post-treatment ones ($P< 0.05$). The effect size (Cohen´s d) for baseline outcomes at the post-treatment follow-up was large (d >0.8) according to Cohens method in all the groups. Comparisons between groups of the baseline and post-treatment follow-up are presented in ***Table 2.***

– CADC (Self-efficacy)

All groups presented statistically significant differences between baseline outcomes and post-treatment ones ($P< 0.05$), except for control group (F=-20.53) and TPE group (F=-27.35). Effect sizes was medium (d=-0.63) for TPE group andsmall in control group (d= -0.37), the rest of the groups shower a large effect size (d >0.8) for baseline and post-treatment follow up outcomes. Comparisons between groups of the baseline and post-treatment follow-up are presented in ***Table 2.***

– PCS (Catastrophizing)

All groups presented statistically significant differences between baseline outcomes and post-treatment ones ($P< 0.01$), except for control group (F= 3.08, $P> 0.05$). The effect size (d) for baseline outcomes at the post-treatment follow-up was large (d >0.8) according to Cohens method in all the groups except for control group in which effect size is small (d=0.31). Comparisons between groups of the baseline and post-treatment follow-up are presented in ***Table 2.***

- Latineen (Drug consumption)

All groups presented statistically significant differences between baseline outcomes and post-treatment ones (*P*< 0.01), except for TPE plus TE plus TMO group (*F*= 0.417, *P*>0.05) and for control group (F=0.00, *P*>0.05). The effect size (d) for baseline outcomes at the post-treatment follow-up was medium in all the groups (d= 0.50 to d=0.79) except for control group which it was voided (d= 0.00). Comparisons between groups of the baseline and post-treatment follow-up are presented in ***Table 2.***

- Beck questionnaire (Depression)

All groups presented statistically significant differences between baseline outcomes and post-treatment ones (*P*< 0.05), except for for TPE plus TE plus TMO group (F=1.60, *P*>0.05) and control group (F=2.60, *P*>0.05). The effect size (Cohen´s d) for baseline outcomes at the post-treatment follow-up was small in all the groups (d= 0.20 to d=0.49). Comparisons between groups of the baseline and post-treatment follow-up are presented in ***Table 2.***

- NDI (Neck Disability)

Only TPE plus TE plus TMO group and control group presented statistically significant differences between baseline outcomes and post-treatment ones (*P*< 0.05). The effect size (d) for baseline outcomes at the post-treatment follow-up was small in all the groups (d= 0.20 to d=0.49) except for control group (d= 0.70) and TPE plus TE plus TMO group (d=0.72) in where effect sizes were medium. Comparisons between groups of the baseline and post-treatment follow-up are presented in ***Table 2.***

All the questionnaires and scales are shown in ANEXES

Variable	**N**	**n group**	**group**	**pre Mean ± SD**	**post Mean ± SD**	**Mean Diff.**	**95% CI**	**Cohens d**
VAS	62	20	0	37.10±31.75	26.40±29.77	10.70*	1.21 to 20.18	0.34
		15	1	38.13±26.69	19.47±22.79	18.66**	7.71 to 29.61	0.75
		15	2	41.80±28.03	24.60±27.39	17.20**	6.25 to 28.14	0.62
		12	3	36.81±29.15	22.92±26.52	5.50	-17.73 to 6,73	0.49
CADC	62	20	0	85.55±52.76	123.50±37.57	-37.95*	-64,49 to -11,41	-0.82

		15	1	74.20±45.74	128.33±31.06	-54.133**	-84.79 to -23.48	-1.38
		14	2	85.93±50.76	113.29±33.47	-27.35	-59.07 to 4.36	-0.63
		13	3	91.08±68.53	111.62±36.92	-20.53	-53.45 to 12.38	-0.37
HIT-6	56	16	0	63.19±10.24	31.69±21.60	31.50**	20.61 to 42.38	1.86
		13	1	64.15±5.32	37.38±22.50	26.76**	14.69 to 38.984	1.63
		15	2	64.27±6.91	38.07±20.35	26.20**	-37.44 to -14.95	1.72
		12	3	64.42±6.27	50.08±19.36	14.33*	1.76 to 26.90	0.98
PCS	54	17	0	21.65±14.39	11.82±10.88	9.82**	5.20 to 14.44	0.99
		12	1	25.58±8.38	13.42±9.56	12.16**	6.66 to 17.66	1.35
		13	2	20.23±9.00	11.69±10.97	8.53**	3.25 to 13.82	0.85
		12	3	19.50±9.73	16.42±10.11	3.08	-2.41 to 8.58	0.31
DRUGS LATINEEN	52	16	0	1.44±1,2	0.81±0.91	0.625**	0.84 to 1.16	0.59
		12	1	1.75±1.05	1.33±0.91	0.417	-2.0 to -0.08	0.42
		14	2	1.71±1.43	1.00±0.87	0.71**	0.13 to 1.29	0.59
		10	3	1.80±1.03	1.80±1.03	0.00	-0.68 to 0.68	0
BECK	39	13	0	14.77±10.45	8.54±7.06	6.23**	2.67 to 9.78	0.69
		10	1	6.40±2.79	4.80±4.70	1.60	-2.45 to 5.65	0.41
		11	2	15.5 ±11.31	10.43±9.61	4.81**	0.95 to 8.68	0.48
		5	3	12.20±8.64	9.60±5.03	2.60	-8.33 to 3.13	0.36
IDC	50	15	0	20.13±12.10	16.13±7.42	4.00	-2.07 to 10.07	0.39
		12	1	26.83±15.36	18.08±7.62	8.75**	1.97 to 15.54	0.72
		13	2	25.54±15.70	20.00±7.73	5.53	-0.98 to 12.06	0.44
		10	3	25.80±14.75	17.90±5.56	7.90*	-15.34 to -0.45	0.70

Table 2: Comparison of changes in primary and secondary variables over time for each treatment group. * P< 0.05 *** P< 0.01 VAS (Pain intensity); CADC (self-efficacy); HIT-6 (quality of life); PCS (Catastrophizing); Drugs Latineen (Drug consumption); BECK (Depression); IDC (cervocal disability); group 0 (TPE+TE); group 1 (TPE+TE+TMO); group 2 (TPE); group 3 (Control group)

4. DISCUSSION

The aim of this study was to determine which one of the biobehavioral combinations of treatments is more effective for quality of life and pain in chronic migraine patients. It has been studied previously in other chronic pain conditions such as chronic neck pain

and also in low back pain, and it has been found that a biobehavioral combination of TPE plus TE plus TMO treatments are effective for the improvement of disability caused and quality of life (Al-Obaidi, Nelson, Al-Awadhi, & Al-Shuwaie, 2000; Beltran-Alacreu, López-de-Uralde-Villanueva, Fernández-Carnero, & La Touche, 2015; Feuerstein & Beattie, 1995; Miller et al., 2010; L. Moseley, 2002).

A migraine patient suffering from an attack, avoid social activities, coping by laying down because an attack is a paroxysmal dysfunction in the brain, from an activation of the trigemino-vascular system originated by a cortical spreading depression (Wieser, Walliser, Womastek, & Kress, 2012). The trigger- avoidance model hypothesis that the avoidance of headache triggers, for example social activities or stress, could result in worsening the disease, sensitize the patient to the triggers and diminished individuals tolerance, thereby affecting her or his quality of life (Paul R Martin & MacLeod, 2009). A biobehavioral approach, as we have used in this study help chronic migraine patients to obtain a satisfactory life even when pain has a high intensity.

There are two systems involved in the experience of pain (G. Bussone & Grazzi, 2013; Gennaro Bussone, Grazzi, & Panerai, 2012) The lateral pain system or neospinothalamic tract (from spinal cord to thalamus and primary somatosensory neocortex) involved in the physical sensation of pain. And the medial pain system, or paleospinothalamic tract (goes through periaqueductal gray and some structures from limbic system) is more related with the affective experiences of pain (Lumley et al., 2011). Both systems comes together at the anterior cingulate cortex which leads to different responses to conflicts, they are conflicts in information processing. Quality of life depends in part of this response to conflicts in our daily life.

The results we have obtained in this study showed that all the groups, even the control one, have improvements in quality of life assessed with Hit-6 questionnaire. We hypothesize that daily life could have pleasant events, for example a new job, having a baby, which do not depend on a biobehavioral treatment and are able to change quality of life.

Sometimes insufficient response to treatment changes pain transforming it into chronic, for this development psychological factors seems to be important, specially when physical changes explaining pain are not evident (Wieser et al., 2012)
We found in our study that pain intensity showed statistical differences between baseline and post-treatment in all the groups except from the control one. It is a favourable outcome because it means that chronic migraine patients treated with a biobehavioral approach show a decrement in pain intensity.

The treatment group that obtain a higher effect size was the combination of TPE plus TE plus TMO. There are several studies that found similar results in chronic neck pain using a very close biobehavioral treatment, even in short and medium term follow up periods (Beltran-Alacreu, López-de-Uralde-Villanueva, et al., 2015; Beltran-Alacreu, Lopez-de-Uralde-Villanueva, et al., 2015).

We should understand that to treat pain effectively , it is important to first understand that it involves an interaction between biological and psychological components (Dahlke, Sable, & Andrasik, 2017). Our treatment combines these interaction adding also the physical part of pain, using manual therapy to assess it.

Confrontation and avoidance are usual responses to pain. In the beginning pain avoidance decreases exposure to pain, while the long term consequence of fear-avoidance coping is disability and maintenance of chronic pain (Vlaeyen & Linton, 2000). The avoidance-endurance model is being demonstrated to be a contributor of chronicity in low back pain. Endurance is characterized by suppressive and maladaptive operant behavior with a low ability to search for social support and an increase of non verbal complaint. (Wieser et al., 2012).

It is important to take into account social rejection, it has been studied in some PET and fMRI studies, and when a person experiences social exclusion, there is an increase of activity in the anterior insula and the anterior cingulate cortex areas related with the emotional and affective experience of pain (DeWall et al., 2010; Eisenberger, 2012; Eisenberger et al., 2003). It is understable that patients with chronic migraine start to have a low self-efficacy and tend to isolation, because CM is more influenced by

emotional factors than somatic ones (Dahlke et al., 2017). We found in our results that the highest effect size obtained was those from the therapeutic education group of patients being medium, probably emotional changes need more time to establish changes in self-efficacy.

Fear, depression, anxiety and avoidance play an important role concerning disability in migraine patients. Depression has been associated with high stress and an important functional impact in daily life, exhibiting it more often chronic migraine patients than episodic ones (Bishop, Holm, Borowiak, & Wilson, 2001; Ford, Calhoun, Kahn, Mann, & Finkel, 2008; Hursey & Jacks, 1992; Juang, Wang, Fuh, Lu, & Su, n.d.; Radat et al., 2008).

We found that only two groups showed differences between pre and post-treatment regarding a reduction in depression, the therapeutic education group and the therapeutic education group plus therapeutic exercise, which have the higher effect size. In a Cochrane revision about physical activity and exercise for chronic pain they found that it carry benefits not only physical but also mental and in physical function (Geneen et al., 2017)

It is known that patients who have anxiety and depression alongside chronic pain showed the most severe pain and pain-related disability, this is why a biobehavioral treatment is a key to improving daily life in chronic migraine patients. We also observed, but did no statistical analysis, in our treated patients with a past trauma, that pain may be exacerbated by unresolved psychological trauma (Dahlke et al., 2017).

The benefits of a behavioral therapy to treat pain, should include a wide vision not only of pain-related behavior but also it is important to take into account patient´s emotions (Dahlke et al., 2017; Jensen & Turk, 2014).

Chronic headaches lead to a perceived headache impact, psychological distress, and use of catastrophizing and avoidance coping strategies as well as a external locus of control (Radat et al., 2008).

We found in our study an improvement between baseline and a month and a half after (post-treatment) in all the groups except from the control one. All treatment groups include a biobehavioral approach, including among others a cognitive behavioral (CB) perspective. In a recent study treating different chronic pain conditions, the authors found that in a 11-week CB therapy program, there were an increase of grey matter in anterior cingulate area and sensoriomotor cortice, areas related with a decrease in pain catastrophizing (Seminowicz et al., 2013). It has been found that grey matter in those areas are reduced in migraines, so our treatment is a clue to increase it (Jin et al., 2013).

Endurance do not let patients ease to their pain adequately, even when it is still mild, though relaxation techniques or an adequate use of medication can decrease pain. The problem is the overuse of medication, it should be considered an essential part of a dysfunctional coping behavior leading with chronicity (Wieser et al., 2012).

We found in our study that the group with the higher effect size was the TE- TPE. It is understable because therapeutic education is made by CBT and education in the neurophysiology of pain as well as a coping strategies and relaxation techniques which have been highly demonstrated to be effective in chronic pain patients, reducing their drug consumption because of feelings of well being (Gallagher et al., 2013; Paula Kindelan-Calvo et al., 2014b; Meeus et al., 2010; F Mongini et al., 2012; G. Lorimer Moseley & Butler, 2015; Trial, Oosterwijck, Meeus, Lambrecht, & Nijs, 2013; WHO Working Group, 1998).

Also therapeutic exercise has been demonstrated to be effective in quality of life, making positive effects and large effect sizes. Nowadays clinicians prescribe physical exercise as well as medication, which has to be well prescribed because, if not, exercise could cause adverse effects (Geneen et al., 2017; Gil-martínez et al., 2013).

A combination of therapeutic patient education, therapeutic exercise and manual therapy have showed an improvement in disability at short and medium term in chronic neck pain patients (Beltran-Alacreu, López-de-Uralde-Villanueva, et al., 2015; Beltran-Alacreu, Lopez-de-Uralde-Villanueva, et al., 2015).

Migraine is associated with mechanical disorder for example a reduction in a cervical range of motion and a presence of miofascial pain syndrome (Ghanbari, Askarzadeh, Petramfar, & Mohamadi, 2015). Trigger points in head and neck are present in patients with migraine, and referral pain associated to trigger points could explain why a migraine attack usually start in the side of the head (Calandre, Hidalgo, García-Leiva, & Rico-Villademoros, 2006). Our approach combining manual therapy, therapeutic exercise and therapeutic education is the most effective one to reduce neck pain and disability. Several studies that include spinal mobilization, relaxation techniques, physiotherapy, and exercise, have demonstrated as our combination of techniques has, a notable improvement in disability in chronic migraine patients (Marcus, Scharff, Mercer, & Turk, 1998; Tuchin, Pollard, & Bonello, 2000).

Our results regarding exercise include motor control, stretching exercises balance and an low intensity aerobic exercise; it is known that exercise produces benefits in migraine patients because it activates the descending pain inhibitory system (Geneen et al., 2017; Gil-martínez et al., 2013).

Manual therapy as well as exercise should be well applied because if it is maladaptive, it is unhelpful when the manual therapy program is based on the biopsychosocial model, as our program is. To design the treatment is very important based on technics in a proper clinical setting (Jones, Edwards, & Gifford, 2002).

CHAPTER 7: Final conclusions

1. CONCLUSION

Migraines have been treated for a long time only by Medical Doctors exclusively using drugs. Drugs used to treat migraine have two disadvantages: On one hand, most of them produce tolerance, which is a phenomenon characterized by the body gradually becoming inured to a drug after it has been taken for a period of time requiring the patient to have a progressively higher dose to obtain the effect for which it has been designed. On the other hand, chronic pain leads to a deterioration of quality of life for the chronification on the physical painful sensations over time. Patients seek help taking a higher quantity of drugs or, even worse, self-medicating. In the US, for example, the rate of drug overdose deaths is a public health problem(Manchikanti, 2007; Park, Saitz, Ganoczy, Ilgen, & Bohnert, 2015).

Nowadays pain knowledge is growing very fast and it has been proved that it is not only a physical feeling but also a psychological, social, biological and behavioral problem. And migraine is one of the most prevalent chronic pain condition around the world, but still little is known about it. There are several theories about its physiopathology, and each one of them propose different modes of treatment. The only thing that holds together the different points of view about migraine, is that it seriously affects the quality of life of people who suffer from it. This was the basis of the present thesis, We wanted to improve the quality of life of patients with migraine from two fundamental perspectives, the physical and the emotional. To achieve this, we had to study other diseases that occur with chronic pain and in this way to begin to think about whether the treatments would be useful for chronic migraine, and to study special features to have a deep knowledge of the origin of migraine.

We realized that physical therapy techniques based on the cognitive behavioral psychological theory, could be very useful, but it has not been enough. Physical therapy approaches, as for example manual therapy, were useful to achieve immediate analgesia, but were not good for migraine patients, so we start using techniques in which the patient has a responsibility. Treatment should be part of his knowledge and effort, so we introduced therapeutic exercise. But it was not enough yet. Patients should know what was happening in their body, they should understand why the pain was more frequent and intense even when the medical tests showed no injury. Then we began to introduce to the therapeutic patient education about neurophysiology of pain. All this began to have an effect on the patients but we still had to address the social and emotional part of the patients and for this we started introducing techniques of relaxation - breathing, stress inoculation and coping - while educating patients to perform more social activities. All always supported by scientific findings in other conditions of chronic pain and, of course, enabling us to demonstrate and apply our hypotheses.

Biobehavioral therapies for pain patients are designed to modify dysfunctional coping strategies. This reduces anxiety, stress and depression and enhances quality of life and sense of personal control, all together reducing the negative impact of the disease on the individual patient. This should be an integral part of the therapeutic management along with adequate medication especially for patients seeking help in clinical centers. We believe that our findings combined with controlled pharmacological support can lead patients with chronic migraine to have an improved quality of life and also greatly reduce pain and greatly improve the disease.

- **Therapeutic exercise as treatment for migraine and tension-type headaches: a systematic review of randomised clinical trials**

The first study has focused on the therapeutic exercise for patients with chronic migraine and tensión type headache. In this review, moderate-limited evidence has been found that therapeutic exercise may reduce the symptoms associated with migraine and/or tension type headaches in the medium term, such as pain intensity and frequency, drug use, improvement of disability and quality of life. Future studies in this same line should use more rigorous research designs in order to extract useful information in

clinical decision making. It is also essential to créate therapeutic exercise interventions with more homogeneous and structured protocols. Research in the area of therapeutic exercise and migraine and/or tension type headache provides important data on non-pharmacological treatments, especially since the studies analyzed in this review have not described any adverse effects.

- **Effectiveness of therapeutic patient education for adults with migraine. A systematic review and meta-analysis of randomized controlled trials.**

This systematic review and meta-analysis found strong evidence for intermediate-term improvements in disability and decreased headache frequency after biobehavioral approaches (BBT) in adult patients with chronic migraine. Moderate evidence was also found with regard to improving the quality of life in the intermediate-term. However, more studies with higher methodological quality and using double blind design are still needed. A direction for future research could be to investigate the long-term effects of migraine treatments with a longitudinal design.

- **Widespread mechanical hyperalgesia and its relationship with psychosocial variables in chronic migraine patients**

This study suggests that there are associations between somatosensory and psychosocial variables in patients suffering from chronic migraines. There are statistically significant differences between chronic migraine patients and healthy subjects in all somatosensory and psychosocial variables except for the kinesiophobia outcome, which suggests that treatment for these patients should not only be physical but also bio-behavioral. Based on our results, widespread mechanical hyperalgesia and its relationship with central sensitization could be the best way to represent the origin of chronic migraine**.** Although our results reveal the presence of widespread mechanical hyperalgesia the central sensitization process in chronic migraine patients should be proved measuring other factors as, for example, mechanical allodynia; additional studies devoted to temporal summation or widespread pain are required to corroborate our findings.

- **Temporal summation, widespread pain and its relationship with psychosocial variables in chronic migraine patients.**

The results of this study support the hypothesis of sensitization of the trigeminocervical complex as the origin for the development of migraines. This study reaffirms the presence of psychosocial factors such as depression, catastrophism and reduced self-efficacy and quality of life, associated with patients with CM, and the exclusion of the presence of kinesiophobia in these patients. Future studies that assess central sensitization with more specific protocols are needed.

- **Biobehavioral Physical Therapy Strategies Based on Therapeutic Exercise Applied to Chronic Migraine Patients**

Differences between experimental groups and the control group were found in chronic migraine patients. A multimodal biobehavioral treatment is a good method for improving quality of life in patients with chronic migraine. A biobehavioral therapy for chronic migraine relies on the successful management of both emotions and, pain related behavior, as well as physical pain in the short term. Therapeutic patient education, therapeutic exercise and manual therapy based on cognitive behavioral therapy combined showed improvements in biopsychosocial variables such as self-efficacy, catastrophizing, drug consumption, depression, pain intensity, quality of life and neck disability in patients with chronic migraine. The combination of behavioral techniques and medication is a good option to improve pain and psychosocial variables in chronic migraine patients.Behavioral therapies are influencing functional and structural changes in the brain

2. LIMITATIONS

The present work has some limitations which we are going to present below. It would be interesting to study more variables related to disability at the psychosocial level to assess the possibility of working in a joint program of physiotherapy and psychology, as well as to generate new data that may serve to propose diagnostic and therapeutic alternatives.

Only short-term follow-up has been measured. It would be interesting to measure the medium and long term effects to see if the results obtained are kept over time or, on the other hand, if it is necessary to carry out reminder and evaluation sessions from time to time.

It would also be interesting to consider the possibility of conducting reliability studies among different therapists when applying treatments to ensure that patients get the same benefits.

Another limitation that has not been taken into account has been to assess patients' adherence to medium- and long-term treatment in order to establish programs that maintain the quality of life over time. We have not evaluated the influence of the disease in the social environment of the patient. Assessing this aspect is important not only to provide the patient with greater safety in terms of their illness and feelings, but also to evaluate future treatment programs that include the participation of the social environment closest to the patient in order to be able to better improve their quality of life and coping strategies and to equip their environment with greater knowledge of the disease and strategies for the patient.

- **First Study**

Studies selected for review lack the use of masking in most cases, this could be taken as a limitation, however it should be considered that clinical trials that rely on bioconductive interventions or therapeutic exercise is very complicated to apply doublé Blind as part of the study design (Dickersin, Chan, Chalmers, Sacks, & Smith Jr., 1987; Rains et al., 2005).

Another limitation of this review has been the language, since the search for articles in the English and Spanish languages has been limited. Optimal revisions should include all studies related to the subject regardless of the languages in which they are written (Gregoire, Derderian, & Le Lorier, 1995; D Moher et al., 1996).

The variability of the exercise itself and the combination of it with other interventions makes it difficult to conclude whether the effects are due to one intervention or another

This systematic review has included migraines and CTT according to the ICHD and perhaps in the future will have to focus on other types of primary headaches to have a broader field of approach and be more specific in the results and treatments

- **Second study**

This study has several limitations. First, our meta-analysis did not include sufficient data to make long-term statistical evaluations. Second, only 8 of the 14 studies included showed acceptable methodological quality, while the other 6 papers had 5 points in the Delphi scale. With reference to methodological quality, it should be noted that two of the nine articles selected for the meta-analysis obtained low methodological quality scores, which may have distorted the results from systematic reviews and meta-analyses. Third, use of the PsychINFO database could lead to bias, owing to the retrieval of unpublished dissertations from North America and the exclusion of other dissertations. Also, there was a lack of information from grey literature, which has not been examined, such as *Conference Papers Index, Dissertation Abstracts* or *System for Information on Grey Literature in Europe (SIGLE).* Fourth, the blinded intervention status was not considered possible in some studies, and it is possible that this led to a variation in results due to special attention and interest received by different groups (known as the Hawthorne effect). Moreover, the fact that patients were volunteers in a few studies could lead to bias. However, according to Rains et al., it seems that applying BBT for headaches is mostly either infeasible or simply not possible; only rarely is blinding meaningfully achievable in the administration of BBT (Rains & Penzien, 2005). The fifth limitation arises from the fact that our research was limited to publications written in English and Spanish, as there are some recent papers in German which have focused on this issue. The sixth limitation is regarding the attrition rates, as Internet-based interventions had greater attrition rates than face-to-face intervention. Finally, the heterogeneity was statistically significant for almost all of the meta-analyses of pain and psychosocial variables, but subgroup analysis could not provide reasons for heterogeneity; therefore, this should be considered a limitation.

- **Third study**

This cross-sectional study had some limitations. First, we did not register the intake of

medication in patients during the measurements. As a result, our findings may have been influenced. We also did not consider medication overuse among chronic migraine patients. However, anxiety and depression have been strongly associated with migraine analgesic medication overuse patients (Usai, Grazzi, D'Amico, Andrasik, & Bussone, 2009). Second, we did not assess craniofacial disabilities. Previous studies have shown that craniofacial disabilities can have an influence on primary headache (Grossi & Lipton, 2009). Additionally, we did not consider neck disabilities, which could be measured using a neck disability index (Papuga, Mesfin, Molinari, & Rubery, 2016). We only measured the spreading of pain by PPT in the tibialis anterior. Additional studies that assess pain expansion are necessary to conclude that patients with chronic migraine present central sensitization.

- **Forth Study**

This study has several limitations. Firstly, we have the homogeneity of the simple (88.46% were women), given that CM has a greater prevalence among the female sex, and the sample size (n=52), which could have affected the result of the correlations. Secondly, the measurements were not performed at the same time for all participants nor could we control the taking of medication. This study assessed the expansion of pain through a body chart; however, we could not compare with healthy participants, given that one of the exclusion criterion was that the healthy participants presented pain. Lastly, we only measured one remote point in the temporal summation: the epicondyle.

- **Fifth Study**

The last study has some limitations. First of all, we only assess short term effects in the study. It would be interesting to study medium and long term periods to observe if the patients need more sessions over time. We did not measure treatment adherence which could give us a wide point of view of the patient's knowledge about the treatment. It would be necessary to study more biobehavioral variables as well as coping, sleeping, and medication consumption in a deeper way. We think that it will be necessary to design a questionnaire to measure how pain influences the patient's job and if the treatment makes an improvement on it. Lastly, we did not assess as well which kind of medication the patients are taking; it is necessary to know which are the best

combinations between biobehavioral and drug treatment to improve chronic migraine.

3. FUTURE PERSPECTIVES

- **STUDY 1: clinical and scientific implications**

Therapeutic exercise has been proven to be a safe and effective therapy to treat migraines. It may be very interesting to study this treatment in other primary headaches and to adapt physical exercise programs in gyms or sports centers where patients could not only improve their pain but also prevent it. Future lines of research could combine multidisciplinary treatments between coaches and physiotherapists for patients with chronic pain. Exercise programs could also be evaluated from a virtual perspective with mobile applications in order to be able to follow up the patient from a distance.

- **STUDY 2: Clinical and scientific implications**

From a clinical perspective, treating patients with migraine should include a biobehavioral therapy (BBT). This is because BBT seems to have a clinical effect in the intermediate-term over disability, quality of life and frequency of migraines. Also, a trend of significant improvement in other variables such as self-efficacy and depression has been observed. Thus, this approach will be particularly indicated when patients present with these characteristics. Our results should be relevant to evidence-based practice with this important population of migraine sufferers. In addition, is important that educational therapy should be targeted as a comprehensive intervention offered to patients. It might be too ambitious to aim for a significant decrease in attack frequency immediately after BBT due to the fact that participants may still be in the process of learning to adapt their lifestyle.

BBT should include educational and activity-based approaches. The educational approach is focused on helping the patient to understand their symptoms from a neurophysiological point of view. Approaches should be used that will lead the patient to return to normal activities through a thorough explanation and graded exposure or graded exercise to reduce fear and severity (Nicholas & George, 2011).

Indeed, there is a general consensus that BBT is not equally suitable for all subjects. Patients who are more likely to benefit include those with chronic or refractory migraine, those with poor coping strategies, and individuals with psychiatric comorbidities such as anxiety and mood disorders. Strong candidates for BBT also include children and adolescents, due to the adverse effects of pharmacological treatments which may be particularly deleterious during growth (Frank Andrasik, 2004; R. A. Nicholson, Buse, Andrasik, & Lipton, 2011). However, the researches designs of the reported studies are still too heterogeneous and too weak to draw definitive conclusions on the effectiveness of BBT.

On the other hand, the attrition rate is something to bear in mind and raises questions about whether participants dropped out of the study for reasons related to either the exposure (website) or the outcome (improvement or worsening of migraine or related symptoms). Future research should attempt to obtain more specific knowledge about potential risks and protective factors to understand the full range of patient experiences when dealing with chronic pain.

- **STUDY 3 and 4: Clinical and scientific implications**

The possible presence of the phenomenon of central sensitization should be considered when treating patients with CM. Nevertheless, we should also consider the presence of the previously mentioned psychosocial factors. Treatment should therefore focus on decreasing the impact of these psychosocial factors and managing the central sensitization. It could be possible to open new lines of research with imaging tests to verify the cortical activation of areas related to the emotions in patients with migraine during an attack.

- **STUDY 5: Clinical and scientific implications**

Future studies with more follow-up periods should be done to better understand how behavioral approaches work on migraine patients and other chronic pain conditions. It is known that behavioral therapies are influencing functional and structural changes in the brain. New studies and research lines are needed for understanding neuroanatomical changes as a function of biobehavioral therapies when applying them to chronic

migraine patients. The present study provides a new vision for the treatment of migraines with novel and safe techniques for patients; future lines of research should include in the treatment people socially close to patients with migraine, in order to be able to improve even more their quality of life, coping strategies and labor productivity.

4. FINAL CONCLUSIONS (ENGLISH VERSION)

Chronic migraine is a complicated disease that affects the quality of life of patients suffering from it. Its origin is very complex and today is still unknown. This work supports the theory of central sensitization as the neurophysiological process that perpetuates migraine chronification. Our hypothesis, which supports the central sensitization as cause, could explain some of the characteristics of the disease.

The results show that the therapeutic exercise is a safe treatment, which has beneficial effects on migraines or tension type headaches and that the therapeutic patient education has proven to be an effective technique, with strong-moderate evidence in the treatment of patients with chronic migraine. The use of these two techniques has been shown to be very positive for the treatment of migraine patients individually.

There is the presence of generalized mechanical hyperalgesia and mechanical allodynia in trigeminal areas and also at a distance in patients with chronic migraine. Its relationship to central sensitization may be the most accurate way to represent the origin of chronic migraine. In addition, significant differences have been found between healthy subjects and patients with chronic migraine as regards somatosensory and psychosocial variables, and associations between these variables in patients with chronic migraine.

There are psychosocial factors, such as a decrease in quality of life, depression, catastrophism, decreased self-efficacy and an absence of kinesiophobia, in patients with chronic migraine. These factors interfere in the day to day lives of the patients who suffer it and therefore it is interesting to investigate treatments that improve these factors to enhance the lives of patients with chronic migraine.

The combination of biopsychosocial techniques such as therapeutic exercise, patient therapeutic education and manual therapy has proven to be a safe and effective

approach with short-term medium-high effect sizes in improving the quality of life of patients with chronic migraine. Future randomized clinical trials with longer follow-ups are needed to conclude that the combination of biopsychosocial techniques are effective in the medium and long term.

CONCLUSIONES GENERALES (Versión en castellano)

La migraña crónica es una enfermedad complicada que afecta a la calidad de vida de los pacientes que la sufren, su origen es muy complejo y hoy en día todavía desconocido , este trabajo apoya la teoría de la sensibilización central como el proceso neurofisiológico que perpetúa la migraña crónica. Nuestra hipótesis que apoya la sensibilización central como causa, podría explicar algunas de las características de la enfermedad.

Los resultados muestran que el ejercicio terapéutico es un tratamiento seguro, que presenta efectos beneficiosos sobre las migrañas o las CTT y la educación terapéutica del paciente ha demostrado ser una técnica efectiva y con una evidencia fuerte-moderada en el tratamiento de pacientes con migraña crónica. El uso de estas dos técnicas se ha demostrado que puede ser muy positivo para el tratamiento de los pacientes con migraña de manera individual.

Existe la presencia de hiperalgesia mecánica generalizada y alodinia mecánica en áreas trigeminales y también a distancia en pacientes con migraña crónica. Su relación con la sensibilización central, podría ser la manera más correcta de representar el origen de la migraña crónica. Además se han encontrado diferencias significativas entre sujetos sanos y pacientes con migraña crónica en cuanto a variables somatosensoriales y psicosociales, y asociaciones entre dichas variables en `pacientes con migraña crónica.

Existen factores psicosociales como un decremento en la calidad de vida, depresión, catastrofismo, disminución de la autoeficacia y una ausencia de kinesiofobia, en pacientes con migraña crónica, estos factores interfieren en el día a día de los pacientes

que la sufren y por tanto es interesante investigar en tratamientos que mejoren estos factores para mejorar la vida de los pacientes con migraña crónica.

La combinación de técnicas biopsicosociales como el ejercicio terapéutico, la educación terapéutica del paciente y la terapia manual, ha demostrado ser un abordaje seguro y efectivo con tamaños del efecto medio-altos a corto plazo en la mejora de la calidad de vida de pacientes con migraña crónica. Se necesitan futuros estudios clínicos aleatorios con mayores seguimientos en el tiempo para concluir que la combinación de técnicas biopsicosociales son efectivas a medio y largo plazo.

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ANNEXES

1. Tampa scale of kinesiophobia (TSK)
2. Self-efficacy scale (CADC)
3. Beck depression inventory (BECK)
4. Drug consumption (Latineen)
5. Cervical disability Index (IDC)
6. Quality of life (Hit 6)
7. Pain Catastrophizing Scale (PCS)

1. TAMPA SCALE OF KINESIOPHOBIA (TSK)

TAMPA SCALE OF KINESIOPHOBIA (Versión corta)

Por favor, señale la respuesta más apropiada a su estado de salud.

	Totalmente desacuerdo	Algo en desacuerdo	Algo de acuerdo	Totalmente de acuerdo
1. Tengo miedo a lesionarme si hago ejercicio	☐	☐	☐	☐
2. Si me dejara vencer por él, el dolor aumentaría	☐	☐	☐	☐
3. Mi cuerpo me está diciendo que tengo algo serio.	☐	☐	☐	☐
4. Tener dolor siempre quiere decir que en el cuerpo hay una lesión.	☐	☐	☐	☐
5. Tengo miedo a lesionarme sin querer.	☐	☐	☐	☐
6. Lo más seguro para evitar que aumente el dolor es tener cuidado y no hacer movimientos innecesarios.	☐	☐	☐	☐
7. No me dolería tanto si no tuviese algo serio en mi cuerpo.	☐	☐	☐	☐
8. El dolor me dice cuándo debo parar la actividad para no lesionarme.	☐	☐	☐	☐
9. No es seguro para una persona con mi enfermedad hacer actividades físicas.	☐	☐	☐	☐
10. No es seguro para una persona con mi enfermedad hacer actividades físicas.	☐	☐	☐	☐
11. Nadie debería hacer actividades físicas cuando tiene dolor.	☐	☐	☐	☐

2. SELF-EFFICACY SCALE (CADC)

Con este cuestionario estamos interesados en conocer la **CAPACIDAD QUE USTED CREE QUE TIENE PARA REALIZAR UNA SERIE DE ACTIVIDADES O TAREAS**. Siguiendo la escala de respuesta que le presentamos, responda poniendo una X en la casilla que usted crea que corresponde a su grado de capacidad.

A continuación, le ponemos un ejemplo; no es necesario que lo conteste.

Por ejemplo, si la pregunta es:
¿Se cree capaz de leer El Quijote?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

Si usted cree que es **totalmente incapaz** de leerlo, tendrá que poner una X en la casilla **0** de la escala de respuesta.

Sin embargo, si usted cree que es **totalmente capaz** de leerlo, tendrá que poner una X en la casilla **10** de la escala de respuesta.

RECUERDE: NO NOS INTERESA SABER SI LO HACE O NO LO HACE. **SÓLO NOS INTERESA SABER SI USTED CREE QUE ES CAPAZ DE HACERLO O NO.**

PONGA UNA X EN EL NÚMERO QUE CORRESPONDA A LA CAPACIDAD QUE CREE QUE TIENE PARA REALIZAR EN ESTE MOMENTO LAS SIGUIENTES ACTIVIDADES O TAREAS.

1 ¿Se cree capaz de controlar su fatiga?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

2 ¿Se cree capaz de regular su actividad, para poder estar activo pero sin empeorar sus síntomas físicos? (por ejemplo, fatiga, dolor)

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

3 ¿Se cree capaz de hacer algo para sentirse mejor si está triste o bajo de ánimo?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

4 Comparado con otra gente con problemas crónicos como los suyos ¿Se cree capaz de controlar su dolor durante sus actividades diarias?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

5 ¿Se cree capaz de controlar sus síntomas físicos, de manera que pueda seguir haciendo las cosas que le gusta hacer?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

6 ¿Se cree capaz de hacer frente a la frustración de sus problemas físicos crónicos?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

7 ¿Se cree capaz de afrontar dolores leves o moderados?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

8 ¿Se cree capaz de afrontar dolores intensos?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

PONGA UNA X EN EL NÚMERO QUE CORRESPONDA A LA CAPACIDAD QUE CREE QUE TIENE PARA REALIZAR LAS SIGUIENTES ACTIVIDADES SIN AYUDA DE OTRA PERSONA. CONSIDERE LO QUE NORMALMENTE PUEDE HACER, NO AQUELLO QUE SUPONGA UN ESFUERZO EXTRAORDINARIO.

1 ¿Se cree capaz de caminar aproximadamente un kilómetro por terreno llano?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

2 ¿Se cree capaz de levantar una caja de aproximadamente 5 Kilos de peso?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

3 ¿Se cree capaz de hacer un programa diario de ejercicios en casa?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

4 ¿Se cree capaz de hacer sus tareas domésticas?

0	1	2	3	4	5	6	7	8	9	10
Me creo totalmente capaz				Me creo moderadamente capaz				Me creo totalmente incapaz		

5 ¿Se cree capaz de participar en actividades sociales?

0	1	2	3	4	5	6	7	8	9	10

Me creo totalmente capaz — Me creo moderadamente capaz — Me creo totalmente incapaz

6 ¿Se cree capaz de ir de compras para adquirir alimentos o ropa?

0	1	2	3	4	5	6	7	8	9	10

Me creo totalmente capaz — Me creo moderadamente capaz — Me creo totalmente incapaz

7 ¿Se cree capaz de cumplir con las mismas obligaciones de trabajo que tenía antes del inicio del dolor crónico? (Para las personas que trabajen en casa, por favor, consideren sus quehaceres domésticos como sus obligaciones)

0	1	2	3	4	5	6	7	8	9	10

Me creo totalmente capaz — Me creo moderadamente capaz — Me creo totalmente incapaz

PONGA UNA X EN EL NÚMERO QUE CORRESPONDA A LA CAPACIDAD QUE CREE QUE TIENE EN ESTE MOMENTO PARA REALIZAR LAS SIGUIENTES ACTIVIDADES:

1 ¿Se cree capaz de disminuir bastante su dolor?

0	1	2	3	4	5	6	7	8	9	10

Me creo totalmente capaz — Me creo moderadamente capaz — Me creo totalmente incapaz

2 ¿Se cree capaz de evitar que el dolor interfiera en su sueño?

0	1	2	3	4	5	6	7	8	9	10

Me creo totalmente capaz — Me creo moderadamente capaz — Me creo totalmente incapaz

3 ¿Se cree capaz de reducir su dolor, aunque sea un poco, haciendo otra cosa que no sea tomar más medicinas?

0	1	2	3	4	5	6	7	8	9	10

Me creo totalmente capaz — Me creo moderadamente capaz — Me creo totalmente incapaz

4 ¿Se cree capaz de reducir mucho su dolor haciendo otra cosa que no sea tomar más medicinas?

0	1	2	3	4	5	6	7	8	9	10

Me creo totalmente capaz — Me creo moderadamente capaz — Me creo totalmente incapaz

3. BECK DEPRESSION INVENTORY (BECK)

En este cuestionario aparecen varios grupos de afirmaciones. Por favor, lea con atención cada una. A continuación, señale cuál de las afirmaciones de cada grupo describe mejor cómo se ha sentido durante esta última semana, incluido en el día de hoy. Si dentro de un mismo grupo, hay más de una afirmación que considere aplicable a su caso, márquela también. Asegúrese de leer todas las afirmaciones dentro de cada grupo antes de efectuar la elección, (se puntuará 0-1-2-3).

1) .

 No me siento triste
 Me siento triste.
 Me siento triste continuamente y no puedo dejar de estarlo.
 Me siento tan triste o tan desgraciado que no puedo soportarlo.

2) .

 No me siento especialmente desanimado respecto al futuro.
 Me siento desanimado respecto al futuro.
 Siento que no tengo que esperar nada.
 Siento que el futuro es desesperanzador y las cosas no mejorarán.

3) .

 No me siento fracasado.
 Creo que he fracasado más que la mayoría de las personas.
 Cuando miro hacia atrás, sólo veo fracaso tras fracaso.
 Me siento una persona totalmente fracasada.

4) .

 Las cosas me satisfacen tanto como antes.
 No disfruto de las cosas tanto como antes.
 Ya no obtengo una satisfacción auténtica de las cosas.
 Estoy insatisfecho o aburrido de todo.

5) .

 No me siento especialmente culpable.
 Me siento culpable en bastantes ocasiones.
 Me siento culpable en la mayoría de las ocasiones.
 Me siento culpable constantemente.

6) .

 No creo que esté siendo castigado.

 Me siento como si fuese a ser castigado.
 Espero ser castigado.
 Siento que estoy siendo castigado.

7) .

 No estoy decepcionado de mí mismo.
 Estoy decepcionado de mí mismo.
 Me da vergüenza de mí mismo.
 Me detesto.

8) .

 No me considero peor que cualquier otro.
 Me autocritico por mis debilidades o por mis errores.
 Continuamente me culpo por mis faltas.
 Me culpo por todo lo malo que sucede.

9) .

 No tengo ningún pensamiento de suicidio.
 A veces pienso en suicidarme, pero no lo cometería.
 Desearía suicidarme.
 Me suicidaría si tuviese la oportunidad.

10) .

 No lloro más de lo que solía llorar.
 Ahora lloro más que antes.
 Lloro continuamente.
 Antes era capaz de llorar, pero ahora no puedo, incluso aunque quiera.

11) .

 No estoy más irritado de lo normal en mí.
 Me molesto o irrito más fácilmente que antes.
 Me siento irritado continuamente.
 No me irrito absolutamente nada por las cosas que antes solían irritarme.

12) .

 No he perdido el interés por los demás.
 Estoy menos interesado en los demás que antes.
 He perdido la mayor parte de mi interés por los demás.
 He perdido todo el interés por los demás.

13) .

 Tomo decisiones más o menos como siempre he hecho.
 Evito tomar decisiones más que antes.

 Tomar decisiones me resulta mucho más difícil que antes.
 Ya me es imposible tomar decisiones.

14) .

 No creo tener peor aspecto que antes.
 Me temo que ahora parezco más viejo o poco atractivo.
 Creo que se han producido cambios permanentes en mi aspecto que me hacen parecer poco atractivo.
 Creo que tengo un aspecto horrible.

15) .

 Trabajo igual que antes.
 Me cuesta un esfuerzo extra comenzar a hacer algo.
 Tengo que obligarme mucho para hacer algo.
 No puedo hacer nada en absoluto.

16) .

 Duermo tan bien como siempre.
 No duermo tan bien como antes.
 Me despierto una o dos horas antes de lo habitual y me resulta difícil volver a dormir.
 Me despierto varias horas antes de lo habitual y no puedo volverme a dormir.

17) .

 No me siento más cansado de lo normal.
 Me canso más fácilmente que antes.
 Me canso en cuanto hago cualquier cosa.
 Estoy demasiado cansado para hacer nada.

18) .

 Mi apetito no ha disminuido.
 No tengo tan buen apetito como antes.
 Ahora tengo mucho menos apetito.
 He perdido completamente el apetito.

19) .

 Últimamente he perdido poco peso o no he perdido nada.
 He perdido más de 2 kilos y medio.
 He perdido más de 4 kilos.
 He perdido más de 7 kilos.
 Estoy a dieta para adelgazar SI/NO.

20) .

 No estoy preocupado por mi salud más de lo normal.

 Estoy preocupado por problemas físicos como dolores, molestias, malestar de estómago o estreñimiento.
 Estoy preocupado por mis problemas físicos y me resulta difícil pensar algo más.
 Estoy tan preocupado por mis problemas físicos que soy incapaz de pensar en cualquier cosa.

21) .

 No he observado ningún cambio reciente en mi interés.
 Estoy menos interesado por el sexo que antes.
 Estoy mucho menos interesado por el sexo.
 He perdido totalmente mi interés por el sexo.

Guía para la interpretación del inventario de la depresión de Beck:

Puntuación Nivel de depresión*

1-10 .....Estos altibajos son considerados normales.
11-16 .....Leve perturbación del estado de ánimo.
17-20 .....Estados de depresión intermitentes.
21-30 .....Depresión moderada.
31-40 .....Depresión grave.
+ 40 .....Depresión extrema.

* Una puntuación persistente de 17 o más indica que puede necesitar ayuda profesional.

4. DRUG CONSUMPTION (LATINEEN)

FECHA / /		
Intensidad del dolor	Nulo Ligero Molesto Intenso Insoportable	0 1 2 3 4
Frecuencia del dolor	No Raramente Frecuente Muy frecuente Continuo	0 1 2 3 4
Consumo de analgésicos	No toma analgésicos Ocasionalmente Regular y pocos Regular y muchos Muchísimos	0 1 2 3 4
Incapacidad	No Ligera Moderada Ayuda necesaria Total	0 1 2 3 4
Horas de sueño	Como siempre Algo peor de lo habitual Se despierta frecuentemente Menos de 4 horas Precisa hipnóticos	0 1 2 3 +1
TOTAL:		

Fig. 1. Cuestionario del índice de Latineen.

5. CERVICAL DISABILITY INDEX (IDC)

Nombre:
Fecha:
Domicilio:
Profesión:
Edad:

Por favor, lea atentamente las instrucciones:

Este cuestionario se ha diseñado para dar información a su médico sobre cómo le afecta a su vida diaria el dolor de cuello. Por favor, rellene todas las preguntas posibles y marque en cada una SÓLO LA RESPUESTA QUE MÁS SE APROXIME A SU CASO. Aunque en alguna pregunta se pueda aplicar a su caso más de una respuesta, marque sólo la que represente mejor su problema.

Pregunta I: Intensidad del dolor de cuello

- ☐ No tengo dolor en este momento
- ☐ El dolor es muy leve en este momento
- ☐ El dolor es moderado en este momento
- ☐ El dolor es fuerte en este momento
- ☐ El dolor es muy fuerte en este momento
- ☐ En este momento el dolor es el peor que uno se puede imaginar

Pregunta II: Cuidados personales (lavarse, vestirse, etc.)

- ☐ Puedo cuidarme con normalidad sin que me aumente el dolor
- ☐ Puedo cuidarme con normalidad, pero esto me aumenta el dolor
- ☐ Cuidarme me duele de forma que tengo que hacerlo despacio y con cuidado
- ☐ Aunque necesito alguna ayuda, me las arreglo para casi todos mis cuidados
- ☐ Todos los días necesito ayuda para la mayor parte de mis cuidados
- ☐ No puedo vestirme, me lavo con dificultad y me quedo en la cama

Pregunta III: Levantar pesos

- ☐ Puedo levantar objetos pesados sin aumento del dolor
- ☐ Puedo levantar objetos pesados, pero me aumenta el dolor
- ☐ El dolor me impide levantar objetos pesados del suelo, pero lo puedo hacer si están colocados en un sitio fácil como, por ejemplo, en una mesa
- ☐ El dolor me impide levantar objetos pesados del suelo, pero puedo levantar objetos medianos o ligeros si están colocados en un sitio fácil
- ☐ Sólo puedo levantar objetos muy ligeros
- ☐ No puedo levantar ni llevar ningún tipo de peso

Pregunta IV: Lectura

- ☐ Puedo leer todo lo que quiera sin que me duela el cuello
- ☐ Puedo leer todo lo que quiera con un dolor leve en el cuello
- ☐ Puedo leer todo lo que quiera con un dolor moderado en el cuello
- ☐ No puedo leer todo lo que quiero debido a un dolor moderado en el cuello
- ☐ Apenas puedo leer por el gran dolor que me produce en el cuello
- ☐ No puedo leer nada en absoluto

Pregunta V: Dolor de cabeza

- ☐ No tengo ningún dolor de cabeza
- ☐ A veces tengo un pequeño dolor de cabeza
- ☐ A veces tengo un dolor moderado de cabeza
- ☐ Con frecuencia tengo un dolor moderado de cabeza
- ☐ Con frecuencia tengo un dolor fuerte de cabeza
- ☐ Tengo dolor de cabeza casi continuo

Pregunta VI: Concentrarse en algo

- ☐ Me concentro totalmente en algo cuando quiero sin dificultad
- ☐ Me concentro totalmente en algo cuando quiero con alguna dificultad
- ☐ Tengo alguna dificultad para concentrarme cuando quiero
- ☐ Tengo bastante dificultad para concentrarme cuando quiero
- ☐ Tengo mucha dificultad para concentrarme cuando quiero
- ☐ No puedo concentrarme nunca

Pregunta VII: Trabajo y actividades habituales

*Pregunta VII: Trabajo**

- ☐ Puedo trabajar todo lo que quiero
- ☐ Puedo hacer mi trabajo habitual, pero no más
- ☐ Puedo hacer casi todo mi trabajo habitual, pero no más
- ☐ No puedo hacer mi trabajo habitual
- ☐ A duras penas puedo hacer algún tipo de trabajo
- ☐ No puedo trabajar en nada

Pregunta VIII: Conducción de vehículos

- ☐ Puedo conducir sin dolor de cuello
- ☐ Puedo conducir todo lo que quiero, pero con un ligero dolor de cuello
- ☐ Puedo conducir todo lo que quiero, pero con un moderado dolor de cuello
- ☐ No puedo conducir todo lo que quiero debido al dolor de cuello
- ☐ Apenas puedo conducir debido al intenso dolor de cuello
- ☐ No puedo conducir nada por el dolor de cuello

Pregunta IX: Sueño

- ☐ No tengo ningún problema para dormir
- ☐ El dolor de cuello me hace perder menos de 1 hora de sueño cada noche
  Pierdo menos de 1 hora de sueño cada noche por el dolor de cuello*
- ☐ El dolor de cuello me hace perder de 1 a 2 horas de sueño cada noche
  Pierdo de 1 a 2 horas de sueño cada noche por el dolor de cuello*
- ☐ El dolor de cuello me hace perder de 2 a 3 horas de sueño cada noche
  Pierdo de 2 a 3 horas de sueño cada noche por el dolor de cuello*
- ☐ El dolor de cuello me hace perder de 3 a 5 horas de sueño cada noche
  Pierdo de 3 a 5 horas de sueño cada noche por el dolor de cuello*
- ☐ El dolor de cuello me hace perder de 5 a 7 horas de sueño cada noche
  Pierdo de 5 a 7 horas de sueño cada noche por el dolor de cuello*

Pregunta X: Actividades de ocio

- ☐ Puedo hacer todas mis actividades de ocio sin dolor de cuello
- ☐ Puedo hacer todas mis actividades de ocio con algún dolor de cuello
- ☐ No puedo hacer algunas de mis actividades de ocio por el dolor de cuello
- ☐ Sólo puedo hacer unas pocas actividades de ocio por el dolor del cuello
- ☐ Apenas puedo hacer las cosas que me gustan debido al dolor del cuello
- ☐ No puedo realizar ninguna actividad de ocio

*Texto utilizado previamente a los cambios propuestos a raíz de los problemas de comprensión.

6. QUALITY OF LIFE (HIT 6)

HIT-6™ TEST SOBRE LOS EFECTOS DEL DOLOR DE CABEZA

Este cuestionario ha sido diseñado para ayudarle a describir y expresar cómo se siente y qué es incapaz de hacer debido al dolor de cabeza.

Para cada pregunta, por favor, marque con una cruz la casilla que corresponda a su respuesta.

1 Cuando usted tiene dolor de cabeza, ¿con qué frecuencia el dolor es intenso?

☐ Nunca ☐ Pocas veces ☐ A veces ☐ Muy a menudo ☐ Siempre

2 ¿Con qué frecuencia el dolor de cabeza limita su capacidad para realizar actividades diarias habituales como las tareas domésticas, el trabajo, los estudios o actividades sociales?

☐ Nunca ☐ Pocas veces ☐ A veces ☐ Muy a menudo ☐ Siempre

3 Cuando tiene dolor de cabeza, ¿con qué frecuencia desearía poder acostarse?

☐ Nunca ☐ Pocas veces ☐ A veces ☐ Muy a menudo ☐ Siempre

4 En las últimas 4 semanas, ¿con qué frecuencia se ha sentido demasiado cansado/a para trabajar o realizar las actividades diarias debido a su dolor de cabeza?

☐ Nunca ☐ Pocas veces ☐ A veces ☐ Muy a menudo ☐ Siempre

5 En las últimas 4 semanas, ¿con qué frecuencia se ha sentido harto/a o irritado/a debido a su dolor de cabeza?

☐ Nunca ☐ Pocas veces ☐ A veces ☐ Muy a menudo ☐ Siempre

6 En las últimas 4 semanas, ¿con qué frecuencia el dolor de cabeza ha limitado su capacidad para concentrarse en el trabajo o en las actividades diarias?

☐ Nunca ☐ Pocas veces ☐ A veces ☐ Muy a menudo ☐ Siempre

▽ + ▽ + ▽ + ▽ + ▽

COLUMNA 1	COLUMNA 2	COLUMNA 3	COLUMNA 4	COLUMNA 5
(6 puntos cada respuesta)	(8 puntos cada respuesta)	(10 puntos cada respuesta)	(11 puntos cada respuesta)	(13 puntos cada respuesta)

Para calcular el resultado final, sume los puntos correspondientes a cada columna.

Por favor, enseñe los resultados de este test (HIT-6) a su médico.

Puntuación total ☐

Cuanto más alta sea la puntuación, obtenida, mayores serán los efectos del dolor de cabeza en su vida.

La puntuación va desde 36 a 78.

TEST SOBRE LOS EFECTOS DEL DOLOR DE CABEZA

¿Qué significa su Puntuación?

Si obtuvo una puntuación de 60 ó más

Sus dolores de cabeza están teniendo un impacto muy severo en su vida. Usted puede estar experimentando dolor que lo inhabilita y otros síntomas que son aún más severos que los de aquéllos otros afectados por dolores de cabeza. No permita que sus dolores de cabeza le impidan disfrutar de las cosas importantes en su vida como la familia, el trabajo, la escuela o las actividades sociales.

Haga una cita **hoy** para que comente los resultados de su HIT-6 y sus dolores de cabeza con su doctor.

Si obtuvo una puntuación entre 56 - 59

Sus dolores de cabeza están teniendo un impacto importante en su vida. Como resultado usted puede estar experimentando dolor severo y otros síntomas, ocasionándole que pierda la oportunidad de pasar el tiempo con la familia, el trabajo, la escuela o en actividades sociales.

Haga una cita **hoy** para que comente los resultados de su HIT-6 y sus dolores de cabeza con su doctor.

Si obtuvo una puntuación entre 50 - 55

Sus dolores de cabeza parecen estar teniendo cierto impacto en su vida. Sus dolores de cabeza no deberían hacerle perder la oportunidad de pasar el tiempo con la familia, el trabajo, la escuela, o en actividades sociales.

Asegúrese de comentar los resultados de su HIT-6 y sus dolores de cabeza en la próxima cita con su doctor.

Si obtuvo una puntuación de 49 ó menos

Sus dolores de cabeza parecen estar teniendo poco o ningún impacto en su vida en este momento. Lo alentamos a que tome el HIT-6 cada mes para continuar el seguimiento de cómo sus dolores de cabeza afectan su vida.

Si su puntuación del HIT-6 es de 50 ó más

Debería compartir los resultados con su doctor. Los dolores de cabeza que están alterando su vida podrían ser migraña.

Lleve consigo el HIT-6 cuando visite a su doctor porque la investigación muestra que cuando los doctores comprenden exactamente qué tan mal afectan los dolores de cabeza la vida de sus pacientes, es más probable que proporcionen un programa de tratamiento exitoso, que pudiera incluir el medicamento.

HIT está disponible también en Internet en www.headachetest.com.

La versión de Internet le permite imprimir el informe personal de sus resultados así como una versión especial detallada de su doctor.

No olvide tomar de nuevo el HIT-6 o intentar la versión de Internet para continuar vigilando su progreso.

Sobre HIT

El Examen del Impacto del Dolor de Cabeza (HIT) es una herramienta utilizada para medir el impacto que los dolores de cabeza tienen en su capacidad para funcionar en el trabajo, la escuela, la casa y en situaciones sociales. Su puntuación le muestra el efecto que los dolores de cabeza tienen en la vida diaria normal y en su capacidad para funcionar. HIT fue desarrollado por un equipo internacional de expertos en dolores de cabeza de neurología y de medicina de cuidados primarios en colaboración con los psicólogos quienes desarrollaron la herramienta de valoración de la salud SF-36®*.

HIT no tiene la intención de ofrecer el consejo médico concerniente al diagnóstico médico o tratamiento. Debería platicar con su proveedor del cuidado de la salud sobre el consejo específico para su caso.

7. PAIN CATASTROPHIZING SCALE (PCS)

ESCALA DE CATASTROFISMO ANTE EL DOLOR (ECD)

Todos los deportistas experimentan situaciones de dolor en algún momento de su carrera deportiva; en muchas ocasiones estas situaciones de dolor están relacionadas con las lesiones sufridas. Esta escala trata de conocer los pensamientos y los sentimientos de los deportistas cuando experimentan dolor.
Todos los datos e información obtenida serán tratados de forma anónima, sirviendo únicamente al objeto de la investigación para la que van dirigidos.

Deporte		Sexo	
Categoría competición		Edad	
Años federado		Puesto en el que juega	
Si actualmente se encuentra lesionado, por favor, cumplimente estas dos cuestiones			
¿Qué lesión tiene?		Tiempo de recuperación estimado	

Por favor, lea con atención y complete con sinceridad marcando de forma clara (con una "X") la opción elegida en cada una de las 13 afirmaciones.
Tomando como referencia la experiencia de dolor presente en su carrera deportiva, indique el grado en el cual experimenta cada uno de los pensamientos o los sentimientos en una escala de 0 (*nunca*) a 4 (*siempre*).
Cuando siento dolor…

SITUACIÓN DE DOLOR	NUNCA	RARA VEZ	ALGUNAS VECES	MUCHAS VECES	SIEMPRE
1. Me preocupo sobre si el dolor se acabará.	0	1	2	3	4
2. Siento que ya no puedo continuar debido al dolor.	0	1	2	3	4
3. El dolor es muy fuerte y creo que nunca va a mejorar.	0	1	2	3	4
4. El dolor es muy desagradable y siento que me supera.	0	1	2	3	4
5. Siento que no aguanto más el dolor.	0	1	2	3	4
6. Tengo miedo de que el dolor pueda ir en aumento.	0	1	2	3	4
7. Me vienen a la memoria experiencias dolorosas anteriores.	0	1	2	3	4
8. Deseo con muchas ganas que el dolor desaparezca.	0	1	2	3	4
9. No paro de pensar en el dolor.	0	1	2	3	4
10. Estoy centrado en cuanto me duele.	0	1	2	3	4
11. Pienso en que lo quiero es que me deje de doler.	0	1	2	3	4
12. No puedo hacer nada para disminuir la intensidad del dolor.	0	1	2	3	4
13. Me pregunto si me podría pasar algo grave.	0	1	2	3	4

Agradecemos su colaboración.